E. In a similar manner, the following compounds were made:

N-(4-fluorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-5-(pyrrolidin-1-yl)methylbenzamide;

N-(4-fluorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-5-(dimethylamino)methylbenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-6-(dimethylamino)methylbenzo[*b*]thien-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((5-((dimethylamino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-5-chlorobenzamid.

F. Other compounds of the invention may be prepared by methods similar to those described in this Example and by methods known to those of ordinary skill in the art.

EXAMPLE 3

Compounds of Formula (Id)

A. To a solution of *N*-(4-chlorophenyl)-2-[((4-(chloromethyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide (0.52 g, 1.1 mmol) in DMF (12 mL) was added sodium thiomethoxide (0.39 g, 5.5 mmol) and the reaction mixture stirred at ambient temperature. After 16 hours, the mixture was poured into water (100 mL) and extracted with ethyl acetate (2x80 mL). The combined organics were washed with water (2x80 mL), 1M hydrochloric acid (2x80 mL) and brine (80 mL), dried over $MgSO_4$ and concentrated of all volatiles *in vacuo*. Purification of the resulting solid by flash chromatography on silica gel afforded 0.36 g (68% yield) of *N*-(4-chlorophenyl)-2-[((3-chloro-4-((methylthio)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide; as a pale yellow solid; NMR (DMSO-d_6) 11.1 (s, 1), 10.8 (s, 1), 8.3 (d, 1), 7.9 (d, 1), 7.8 (s, 1), 7.7 (d, 2), 7.6 (dd, 1), 7.4 (d, 2), 3.7 (s, 2), 2.0 (s, 3) ppm.

B. In a similar manner, the following compounds were made:

N-(4-chlorophenyl)-2-[((3-chloro-5-((methylthio)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide; NMR ($CDCl_3$) 11.0 (s, 1), 9.2 (s, 1), 8.1 (d, 1), 7.8 (d, 2), 7.5 (d, 1), 7.4 (d, 2), 7.1 (dd, 1), 6.9 (s, 1), 3.8 (s, 2), 2.1 (s, 3) ppm;

N-(4-chlorophenyl)-2-[((3-chloro-5-((imidazol-1-yl)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide; NMR (DMSO-d_6) 11.1 (s, 1), 10.7 (s, 1), 9.2 (s, 1), 8.3 (d, 1), 7.9 (d, 1), 7.8 (s, 1), 7.3-7.2 (m, 4), 7.4 (s, 1), 7.3 (s, 2), 5.6 (s, 2) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-cyanomethyl-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.4 (s, 1), 8.3 (s, 1), 8.1 (d, 1),

7.8 (m, 2), 7.3 (s, 1), 7.2 (s, 1), 3.9 (s, 2), 3.8 (s, 3) ppm.

C. In a manner similar to that described in Paragraph A above, *N*-(4-chlorophenyl)-2-[((4-(chloromethyl)-3-chlorothiophen-2-yl)carbonyl)amino]-5-chlorobenzamide (0.30 g, 0.64 mmol) reacted with sodium imidazole (0.17 g, 1.9 mmol) in DMF (10 mL) to afford *N*-(4-chlorophenyl)-2-[((3-chloro-4-((imidazol-1-yl)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide. Purification by HPLC on a C18 Dynamax column with acetonitrile in water gradient with 0.1% trifluoroacetic acid afforded two products: The earlier eluting material afforded *N*-(4-chlorophenyl)-2-[((3-chloro-4-((imidazol-1-yl)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide, trifluoroacetic acid salt as a cream-colored solid; NMR (DMSO-d_6/TFA) 11.1 (s, 1), 10.8 (s, 1), 9.2 (s, 1), 8.3 (d, 1), 8.1 (s, 1), 7.9 (d, 1), 7.7 (m, 5), 7.4 (d, 2), 5.4 (s, 2) ppm. The later eluting material afforded *N*-(4-chlorophenyl)-2-[((3-chloro-4-(hydroxymethyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide; as a white solid; NMR (DMSO-d_6/TFA) 11.1 (s, 1), 10.8 (s, 1), 8.3 (d, 1), 7.9 (d, 1), 7.8 (s, 1), 7.7 (d, 2), 7.6 (dd, 1), 7.4 (d, 2), 5.4 (br, 1), 4.4 (s, 2) ppm.

D. To a solution of 1,2,4-triazole (0.40 g, 5.7 mmol) in DMF (10 mL) was added NaH (60% dispersion in mineral oil, 0.23 g, 5.7 mmol) and the mixture stirred at ambient temperature. After 10 min, *N*-(4-chlorophenyl)-2-[((4-(chloromethyl)-3-chlorothiophen-2-yl)carbonyl)amino]-5-chlorobenzamide (0.90 g, 1.9 mmol) in DMF (5 mL) was added and stirring continued. After 18 hours, the mixture was poured onto water and extracted with methylene chloride. The organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash chromatography on silica gel afforded 0.99 g (77% yield) of *N*-(4-chlorophenyl)-2-[((3-chloro-4-((1,2,4-triazol-1-yl)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide; as a white solid; NMR (DMSO-d_6/TFA) 11.2 (s, 1), 10.7 (s, 1), 9.3 (s, 1), 8.5 (s, 1), 8.3 (d, 1), 8.0 (s, 1), 7.9 (d, 1), 7.7 (d, 2), 7.6 (dd, 1), 7.4 (d, 2), 5.5 (s, 2) ppm.

E. In a similar manner, the following compounds were made:

N-(4-chlorophenyl)-2-[((3-chloro-4-((tetrazol-1-yl)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide; NMR (DMSO-d_6/TFA) 11.2 (s, 1), 10.7 (s, 1), 9.4 (s, 1), 8.3 (d, 1), 8.0 (s, 1), 7.85 (d, 1), 7.7 (d, 2), 7.5 (dd, 1), 7.3 (d, 2), 5.7 (s, 2) ppm;

N-(4-chlorophenyl)-2-[((3-chloro-4-((tetrazol-2-yl)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide; NMR (DMSO-d_6/TFA) 11.2 (s, 1), 10.7 (s, 1), 9.4 (s, 1), 8.3 (d, 1), 8.1 (s, 1), 7.9 (d, 1), 7.7 (d, 2), 7.6 (dd, 1), 7.4 (d, 2), 5.9 (s, 2) ppm;

N-(4-chlorophenyl)-2-[((3-chloro-4-((pyrazol-1-yl)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide; NMR (DMSO-d_6/TFA) 11.1 (s, 1), 10.7 (s, 1), 7.3-8.4 (m, 10), 6.3 (s, 1), 5.3 (s, 2) ppm;

N-(4-chlorophenyl)-2-[((3-chloro-4-((1,2,3-triazol-1-yl)methyl)thiophen-2-yl)carbonyl)amino]-5-

chlorobenzamide; NMR (DMSO-d_6/TFA) 11.1 (s, 1), 10.7 (s, 1), 7.3-8.4 (m, 9), 5.3 (s, 2) ppm;

N-(4-chlorophenyl)-2-[((3-chloro-4-((1,2,3-triazol-2-yl)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide; NMR (DMSO-d_6/TFA) 11.2 (s, 1), 10.9 (s, 1), 7.3-8.5 (m, 10), 5.6 (br s, 2) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-(2-imino-3-methyl-5-oxoimidazolin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.5 (br s., 1), 9.4 (s, 1), 8.4 (d, 1), 8.1 (d, 1), 7.9 (m, 2), 7.4 (s, 1), 7.3 (m, 2), 4.5 (d, 2), 4.2 (s, 2), 3.9 (s, 3), 3.1 (s, 3) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((4,5-dichloroimidazol-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide; NMR (DMSO-d_6/TFA) 10.85 (s, 1), 9.40 (s, 1), 8.30 (d, 1), 8.10 (d, 1), 7.80-7.86 (m, 2), 7.65 (s, 1), 7.30 (d, 1), 7.25 (d, 1), 5.20 (s, 2), 3.80 (s, 3) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((2-methyl-4-nitroimidazol-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide; NMR (DMSO-d_6/TFA) 10.85 (s, 1), 9.40 (s, 1), 8.30 (d, 1), 8.20 (s, 1), 8.10 (d, 1), 7.80 (dd, 1), 7.70 (s, 1), 7.30 (d, 1), 7.25 (d, 1), 5.20 (s, 2), 3.80 (s, 3), 2.30 (s, 3) ppm.

F. To a solution of *N*-(4-chlorophenyl)-2-[((4-(chloromethyl)-3-chlorothiophen-2-yl)carbonyl)amino]-5-chlorobenzamide (0.70 g, 1.5 mmol) in DMF (5 mL) was added 2-(dimethylamino)ethanethiol (2.1 g, 15 mmol), followed by potassium carbonate (1.0 g, 7.2 mmol) and the reaction stirred at ambient temperature. After 24 hours, the mixture was poured into water (100 mL) and the resulting solid collected by filtration, washed with water and dried *in vacuo*. Purification by flash chromatography on silica gel afforded 0.28 g (35% yield) of *N*-(4-chlorophenyl)-2-[((3-chloro-4-(((2-(dimethylamino)ethyl)thio)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide; as a cream-colored solid; NMR (DMSO-d_6) 11.1 (s, 1), 10.8 (s, 1), 8.3 (d, 1), 7.9 (d, 1), 7.8 (s, 1), 7.7 (d, 2), 7.6 (dd, 1), 7.4 (d, 2), 3.7 (s, 2), 2.5 (t, 2), 2.4 (t, 2), 2.1 (s, 6) ppm.

G. In a similar manner, the following compounds were made:

N-(4-chlorophenyl)-2-[((3-chloro-4-(((methoxycarbonylmethyl)thio)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide; NMR (DMSO-d_6) 11.1 (s, 1), 10.8 (s, 1), 8.3 (d, 1), 7.9 (d, 1), 7.8 (s, 1), 7.7 (d, 2), 7.6 (dd, 1), 7.4 (d, 2), 3.8 (s, 2), 3.6 (s, 3) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((4,5-dihydropyrazolin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.4 (s, 1), 8, 4 (s, 1), 8.1 (d, 1), 7.9 (m, 2), 7.4 (s, 1), 7.2 (d, 2), 4.2 (s, 2), 3.9 (s, 3), 3.1 (t, 2), 2.7 (t, 2) ppm;

N-(4-chlorophenyl)-2-[((3-chloro-5-(((methoxycarbonylmethyl)thio)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide; NMR (DMSO-d_6) 11.0 (s, 1), 10.8 (s, 1), 8.3 (d, 1), 7.9 (s, 1), 7.8 (d, 2), 7.6 (dd, 1), 7.4 (d, 2), 7.1 (s, 1), 4.1 (s, 2), 3.6 (s, 3), 3.4 (s, 2) ppm;

N-(4-chlorophenyl)-2-[((3-chloro-6-((methoxycarbonyl)methylthio)methylbenzo[*b*]thien-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((pyrazol-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide; NMR (DMSO-d_6) 10.9 (s, 1H), 9.40 (s, 1H), 8.36 (d, 1H), 8.10 (d, 1H), 7.90 (dd, 1H), 7.78 (d, 1H), 7.66 (s, 1H), 7.46 (d, 1H), 7.38 (d, 1H), 7.26 (d, 1H), 6.30 (s, 1H), 5.35 (s, 2H), 3.83 (s, 3H) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((hydantoin-3-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide; NMR (DMSO-d_6) 10.82 (s, 1H), 9.40 (s, 1H), 8.36 (d, 1H), 8.18 (s, 1H), 8.10 (d, 1H), 7.90 (dd, 1H), 7.70 (s, 1H), 7.38 (d, 1H), 7.27 (d, 1H), 4.46 (s, 2H), 3.97 (s, 2H), 3.88 (s, 3H) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((2-(ethylimino)pyrrolidin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.4 (d, 1), 9.3 (m, 1), 8.4 (d, 1), 8.1 (d, 1), 8.0 (s, 1), 7.9 (m, 2), 7.4 (d, 1), 7.3 (d, 1), 4.6 (s, 2), 3.9 (s, 3), 3.6 (t, 2), 3.4 (m, 2), 3.0 (t, 3), 2.1 (m, 2), 1.2 (t, 3) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((2-iminopiperidin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.3 (d, 1), 9.1 (s, 1), 8.6 (br s, 1), 8.3 (d, 1), 8.1 (d, 1), 7.9 (dd, 1), 7.6 (d, 1), 7.4 (d, 1), 7.3 (d, 1), 4.6 (s, 2), 3.9 (s, 3), 3.4 (m, 2), 2.7 (m, 2), 1.9 (m, 4) ppm.

H. To 2-methoxyethanol (20 mL) at 0°C was added NaH (0.45 g, 11 mmol). The solution was warmed to ambient temperature and stirred for 16 hours. *N*-(5-chloropyridin-2-yl)-2-[((4-(chloromethyl)-3-chlorothiophen-2-yl)carbonyl)amino]--3-methoxy-5-chlorobenzamide (1.0 g, 2.3 mmol) was added and stirring continued for 3 hours. The mixture was then heated at 65°C for 4 hours, then poured onto ice water (200 mL). The resulting solid was collected by filtration, washed with water and 50% ether/hexanes, and dried *in vacuo* to afford 0.65 g (52% yield) of *N*-(4-chlorophenyl)-2-[((3-chloro-4-((2-(2-methoxyethoxy)ethoxy)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide; as a pale yellow solid: NMR (DMSO-d_6/TFA) 11.1 (s, 1), 10.7 (s, 1), 8.3 (d, 1), 7.9 (d, 2), 7.7 (d, 2), 7.6 (d, 1), 7.4 (s, 1), 7.4 (s, 1), 4.4 (s, 2), 3.5 (m, 6), 3.4 (m, 2), 3.2 (s, 3) ppm.

I. In a similar manner, the following compounds were made:

N-(4-chlorophenyl)-2-[((3-chloro-4-((2-(2-(2-methoxyethoxy)ethoxy)ethoxy)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide; NMR (DMSO-d_6) 11.2 (s, 1), 10.8 (s, 1), 8.4 (d,

1), 7.9 (s, 1), 7.8 (s, 1), 7.7 (d, 2), 7.6 (d, 1), 7.4 (d, 2), 4.4 (d, 2), 3.6 (m, 4), 3.5 (m, 6), 3.4 (m, 2), 3.2 (s, 3) ppm;

N-(4-chlorophenyl)-2-[((3-chloro-4-((2-methoxyethoxy)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-4-(((2,2-dimethyldioxolan-4-yl)methoxy)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide; NMR (DMSO-d_6) 11.1 (s, 1), 10.8 (s, 1), 8.3 (d, 1), 8.0 (d, 2), 7.7 (d, 2), 7.6 (d, 1), 7.4 (d, 2), 4.5 (s, 2), 4.2 (t, 1)4.0 (t, 1), 3.6 (m, 1), 3.4 (d, 2), 1.2 (d, 6) ppm.

J. In a manner similar to that described in Paragraph F above, to a solution of 3-dimethylamino-5-methylpyrazole (0.38 g, 3.0 mmol), *N*-(5-chloropyridin-2-yl)-2-[((4-(chloromethyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide (1.0 g, 2.0 mmol), and DMSO (10 mL) was added K_2CO_3 (1.0 g, 7.2 mmol). The mixture was stirred at ambient temperature for 16 hours, then it was poured into H_2O. The solid was isolated by filtration. Purification by HPLC on a C18 Dynamax column with 25-95% acetonitrile in water gradient with 0.1% trifluoroacetic acid afforded the trifluoroacetic acid salts of *N*-(5-chloropyridin-2-yl)-2-[((4-((3-dimethylamino-5-methylpyrazol-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide; NMR (DMSO-d_6) 10.90 (s, 1H), 9.50 (s, 1H), 8.40 (d, 1H), 8.10 (d, 1H), 7.90 (dd, 1H), 7.60 (s, 1H), 7.40 (d, 1H), 7.25 (d, 1H), 6.45 (s, 1H), 4.90 (s, 2H), 3.90 (s, 3H), 2.50 (s, 6H), 2.25 (s, 3H) ppm, and *N*-(5-chloropyridin-2-yl)-2-[((4-((3-dimethylamino-5-methylpyrazol-2-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide; NMR (DMSO-d_6) 10.90 (s, 1H), 9.40 (s, 1H), 8.40 (d, 1H), 8.10 (d, 1H), 7.90 (dd, 1H), 7.38 (s, 1H), 7.28 (d, 1H), 7.25 (d, 1H), 5.60 (s, 1H), 5.00 (s, 2H), 3.90 (s, 3H), 2.70 (s, 3H), 2.20 (s, 3H) ppm.

K. In a similar manner, the following compound was made:

N-(5-chloropyridin-2-yl)-2-[((4-((5-aminotetrazol-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.4 (s., 1), 8.3 (d, 1), 8.1 (d, 1), 7.9 (dd, 2), 7.7 (s, 1), 7.3 (d, 1), 7.2 (d, 1), 5.3 (s, 1), 3.9 (s, 3) ppm.

L. In a manner similar to that described in Paragraph J above, to a solution of *N,N*-diethylhydroxylamine (0.45 g, 5.0 mmol), *N*-(5-chloropyridin-2-yl)-2-[((4-(chloromethyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide (0.51 g, 1.0 mmol), and DMSO (10 mL) was added K_2CO_3 (0.68 g, 4.9 mmol). The mixture was stirred at 40°C for 2 days, then it was poured into water. The resulting mixture was extracted with CH_2Cl_2 (2x50 mL). The organic layer was washed with 1% K_2CO_3, brine, treated with charcoal and concentrated. Purification by silica gel chromatography using 10:1 CH_2Cl_2:CH_3OH with 1%

NH_4OH followed by precipitation from CH_2Cl_2 and hexane afforded *N*-(5-chloropyridin-2-yl)-2-[((4-(((diethylamino)oxy)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, as a white solid; NMR (DMSO-d_6) 8.35 (s, 1H), 8.20 (s, 1H), 8.10 (d, 1H), 7.90 (dd, 1H), 7.35 (s, 1H), 7.30 (s, 1H), 4.20 (s, 2H), 3.85 (s, 3H), 3.20-2.80 (m, 4H), 1.20 (t, 6H) ppm.

M. In a similar manner, the following compound was made:

N-(5-chloropyridin-2-yl)-2-[((4-((3-amino-1,2,4-triazol-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.4 (s., 1), 8.4 (d, 1), 8.3 (m, 2), 8.1 (d, 1), 7.9 (dd, 1), 7.7 (s, 1), 7.4 (s, 1), 7.3 (s, 1), 5.1 (s, 2), 3.9 (s, 3) ppm.

N. In a manner similar to that described above in Paragraph F, to a solution of 2-methyl-4,5-dihydroimidazole (1.50 g, 17.8 mmol), *N,N*-diethylhydroxylamine (0.45 g, 5.0 mmol), *N*-(5-chloropyridin-2-yl)-2-[((4-(chloromethyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide (2.00 g, 4 mmol) and DMF (15 mL) was added K_2CO_3 (2.50 g, 18.1 mmol). The mixture was stirred at ambient temperature for 16 hours. Purification by HPLC on a C18 Dynamax column with 20-50% acetonitrile in water gradient with 0.1% trifluoroacetic acid afforded the trifluoroacetic acid salt of *N*-(5-chloropyridin-2-yl)-2-[((4-((2-methylimidazolin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt, as a white solid; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 10.2 (s, 1), 9.4 (s, 1), 8.3 (s, 1), 8.1 (d, 1), 8.0 (s, 1), 7.8 (d, 1), 7.3 (s, 1), 7.2 (s, 1), 4.6 (s, 2), 3.8 (s, 3), 3.7 (s, 4), 2.3 (S, 3) ppm.

O. In a similar manner, the following compounds were made:

N-(5-chloropyridin-2-yl)-2-[((4-((4-amino-5-(aminocarbonyl)imidazol-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.4 (s, 1), 8.8 (s, 1), 8.4 (d, 1), 8.1 (dd, 1), 7.9 (dd, 1), 7.8 (s, 1), 7.4 (d, 1), 7.3 (d, 1), 5.3 (s, 2), 3.9 (s, 3) ppm; and

N-(5-chloropyridin-2-yl)-2-[((4-((2-iminopiperidin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.3 (d, 1), 9.1 (s, 1), 8.6 (br s, 1), 8.3 (d, 1), 8.1 (d, 1), 7.9 (dd, 1), 7.6 (d, 1), 7.4 (d, 1), 7.3 (d, 1), 4.6 (s, 2), 3.9 (s, 3), 3.4 (m, 2), 2.7 (m, 2), 1.9 (m, 4) ppm.

P. In a similar manner to that described in Paragraph F above, to a solution of theobromine (1.06 g, 5.9 mmol), *N,N*-diethylhydroxylamine (0.45 g, 5.0 mmol), *N*-(5-chloropyridin-2-yl)-2-[((4-(chloromethyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide (0.32 g, 0.6 mmol), and DMF (40 mL) was added K_2CO_3 (0.74 g, 5.3 mmol).

The mixture was stirred at 40°C for 6 days, then it was poured into water. The solid was isolated by filtration. Purification by recrystallization from CH_2Cl_2 and CH_3OH afforded *N*-(5-chloropyridin-2-yl)-2-[((4-((2,3,4,5,6,7-hexahydro-3,7-dimethyl-2,6-dioxo-1*H*-purin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, as a white solid; NMR (DMSO-d_6) 10.90 (s, 1H), 9.40 (s, 1H), 8.36 (d, 1H), 8.12 (d, 1H), 8.06 (s, 1H), 7.90 (dd, 1H), 7.55 (s, 1H), 7.38 (d, 1H), 7.27 (d, 1H), 4.97 (s, 2H), 3.90 (s, 6H), 3.40 (s, 3H) ppm.

Q. In a manner similar to that described in Paragraph P above, a mixture of cytosine (0.3 g, 3.0 mmol), *N*-(5-chloropyridin-2-yl)-2-[((4-(chloromethyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide (0.25 g, 0.5 mmol), cesium carbonate (0.5 g, 1.5 mmol), and DMF (5 mL) was heated under N_2 at 60°C for 15 hours. The mixture was cooled in ice bath, and trifluoroacetic acid (0.5 mL) was added dropwise. Purification by HPLC on a C18 Dynamax column with 20-70% acetonitrile in water gradient with 0.1% trifluoroacetic acid gave 0.17 g of the trifluoroacetic acid salt of *N*-(5-chloropyridin-2-yl)-2-[((4-((5-amino-2-oxo-2*H*-pyrimidin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt, as a white solid; NMR (DMSO-d_6, 40°C) 10.75 (s, 1), 9.35 (s, 1), 9.30 (b, 1), 8.35 (b, 1), 8.30 (d, 1), 8.05 (d, 1), 7.95 (d, 1), 7.85 (dd, 1), 7.90 (s, 1), 7.35 (d, 1), 7.25 (d, 1), 6.00 (d, 1), 4.90 (s, 2), 3.85 (s, 3) ppm.

R. In a similar manner, the following compounds were made:

N-(5-chloropyridin-2-yl)-2-[((4-((6-aminopurin-9-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt, and *N*-(5-chloropyridin-2-yl)-2-[((4-((6-aminopurin-7-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.75 (s, 0.5), 10.74 (s, 0.5), 9.35 (m, 1.5), 8.83 (s, 0.5), 8.82 (b, 0.5), 8.55 (s, 0.5), 8.30 (m, 1.5), 8.27 (s, 0.5), 8.12 (b, 1), 8.06 (d, 1), 7.86 (m, 1, 5), 7.70 (s, 1), 7.34 (t, 1), 7.25 (t, 1), 5.56 (s, 1), 5.35 (s, 1), 3.80 (s, 3) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((2-amino-6-oxopurin-9-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt, and *N*-(5-chloropyridin-2-yl)-2-[((4-((2-amino-6-oxopurin-7-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6) 10.75 (s, 1), 10.65 (s, 0.5), 9.33 (s, 1), 8.38 (s, 0.5), 8.31 (t, 1), 8.06 (dd, 1), 7.91 (s, 0.5), 7.88 (dd, 0.5), 7.86 (dd, 0.5), 7.69 (s, 0.5), 7.50 (s, 0.5), 7.34 (d, 1), 7.25 (d, 1), 6.75 (b, 1), 6.50 (b, 1), 5.40 (s, 1), 5.10 (s, 1), 3.85 (s, 3) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((2-amino-4-imino-1,4-dihydropyrimidin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid

salt; NMR (DMSO-d_6/TFA) 10.80 (s, 1), 9.35 (s, 1), 8.33 (d, 1), 8.22 (s, 1), 8.10 (s, 1), 8.07 (d, 1), 8.10 (s, 2), 7.88 (dd, 1), 7.72 (d, 1), 7.65 (s, 1), 7.36 (d, 1), 7.26 (d, 1), 6.40 (d, 1), 5.00 (s, 2), 3.85 (s, 3) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-(imino(thiophen-2-yl)methyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.85 (s, 1), 10.10 (s, 1), 9.60 (s, 1), 9.40 (s, 1), 9.20 (s, 1), 8.29 (d, 1), 8.10 (d, 1), 8.00 (dd, 1), 7.91 (dd, 1), 7.84 (s, 1), 7.82 (dd, 1), 7.30 (d, 1), 7.26 (m, 2), 4.55 (d, 2), 3.80 (s, 3) ppm; and

N-(5-chloropyridin-2-yl)-2-[((4-((2,4-diamino-6-hydroxypyrimidin-5-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.85 (s, 1), 9.30 (s, 1), 8.30 (d, 1), 8.10 (d, 1), 8.00 (b, 1), 7.80 (dd, 1), 7.35 (s, 1), 7.30 (s, 1), 7.25 (s, 1), 3.80 (s, 3), 3.40 (s, 2) ppm.

S. In a manner similar to that described in Paragraph D, to a solution of benzamidine hydrochloride (0.78 mg, 5 mmol) and DMF (10 mL) was added NaH (0.21 g, 5.2 mmol). The mixture was stirred at ambient temperature for 30 minutes. The mixture was cooled to 0°C, then *N,N*-diethylhydroxylamine (0.45 g, 5.0 mmol), *N*-(5-chloropyridin-2-yl)-2-[((4-(chloromethyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide (0.51 mg, 1 mmol) was added. The mixture was allowed to warm to ambient temperature and stirred for 5 days. The mixture was added to water and the resulting precipitate was isolated by filtration. Purification by HPLC on a C18 Dynamax column with 25-95% acetonitrile in water gradient with 0.1% trifluoroacetic acid afforded the trifluoroacetic acid salt of *N*-(5-chloropyridin-2-yl)-2-[((4-((*N*'-(imino(phenyl)methyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide; NMR (DMSO-d_6) 10.90 (s, 1H), 10.10 (br s, 1H), 9.65 (br s, 1H), 9.40 (s, 1H), 9.25 (br s, 1H), 8.40 (d, 1H), 9.10 (d, 1H), 7.95 (s, 1H), 7.90 (dd, 1H), 7.80-7.70 (m, 3H), 7.65-7.59 (m, 2H), 7.40 (d, 1H), 7.30 (d, 1H), 4.55 (s, 2H), 3.85 (s, 3H) ppm.

T. In a similar manner, the following compounds were made:

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-(1-imino-2-(aminocarbonyl)ethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6) 10.90 (s, 1H), 9.40 (s, 1H), 8.90 (s, 2H), 8.70 (s, 2H), 8.40 (d, 1H), 8.10 (d, 1H), 7.90 (dd, 1H), 7.70 (s, 1H), 7.60 (s, 1H), 7.58 (s, 1H), 7.40 (s, 1H), 7.25 (s, 1H), 3.90 (s, 3H), 3, 80 (m, 2H), 3.20 (m, 2H) ppm; and

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-(cyclopropyl(imino)methyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6) 10.90 (s, 1H), 8.60 (br s, 1H), 9.38 (s, 1H), 8.70 (br s, 1H), 8.38 (d, 1H),

8.10 (d, 1H), 8.00-7.80 (m, 2H), 7.40 (d, 1H), 7.25 (d, 1H), 4.40 (s, 2H), 3.90 (s, 3H), 1.98-1.85 (m, 1H), 1.20-1.10 (m, 4H) ppm.

U. Other compounds of the invention may be prepared by methods similar to those described in this Example and by methods known to those of ordinary skill in the art.

EXAMPLE 4

Compounds of Formula (If)

A. To a solution of *N*-(5-chloropyridin-2-yl)-2-[(4-((methylamino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide (1.3g, 2.5 mmol) in pyridine (20 mL) at 0°C was added methanesulfonyl chloride (0.20 mL, 2.8 mmol). The solution was allowed to warm to ambient temperature with stirring. After 16 hours, the pyridine was removed *in vacuo*. The resulting oil was purified by flash chromatography on silica gel to afford 1.1 g (75% yield) of *N*-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(methylsulfonyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, as a white solid; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.4 (s, 1), 8.3 (s, 1), 8.1 (d, 1), 7.9 (d, 1), 7.8 (s, 1), 7.4 (s, 1), 7.3 (s, 1), 4.2 (s, 2), 3.9 (s, 3), 3.0 (s, 3), 2.7 (s, 3) ppm.

B. In a similar manner, the following compounds were made:

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methylsulfonyl-*N*'-(2-(pyrrolidin-1-yl)ethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(morpholin-4-yl)-5-chlorobenzamide; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.5 (s, 1), 7.3-8.5 (m, 6), 4.3 (s, 2), 2.8-4.1 (m, 14), 2.5 (s, 3), 2.2 - 2.5 (m, 2), 1.0-1.2 (m, 4) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-((dimethylamino)sulfonyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.4 (s, 1), 8.4 (s, 1), 8.1 (d, 1), 7.9 (d, 1), 7.8 (s, 1), 7.4 (s, 1), 7.3 (s, 1), 4.3 (s, 2), 3.9 (s, 3), 2.8 (s, 6), 2.7 (s, 3) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-((3,5-dimethylisoxazol-4-yl)sulfonyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.4 (s, 1), 8.4 (s, 1), 8.1 (d, 1), 7.9 (d, 1), 7.8 (s, 1), 7.4 (s, 1), 7.3 (s, 1), 4.3 (s, 2), 3.9 (s, 3), 2.7 (s, 3), 2.6 (s, 3), 2.4 (s, 3) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-(methyl)sulfonyl-*N*'-(2-(dimethylamino)ethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.5 (s, 1), 9.4 (s, 1), 8.4 (s, 1), 8.1 (d, 1), 7.9 (s, 1), 7.9 (d, 1), 7.4 (s, 1), 7.3 (s, 1), 4.2 (s, 2), 3.9 (s, 3), 3.6 (m, 2), 3.2 (m, 2), 3.1 (s, 3), 2.8 (s, 6) ppm; and

N-(5-chloropyridin-2-yl)-2-[((4-((((2-chloroethyl)sulfonyl)amino)methyl)-3-chlorothiophen-2-

yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide.

C. In a similar manner to that described in Paragraph A above, *N*-(5-chloropyridin-2-yl)-2-[((4-((methylamino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(4-methylpiperazin-1-yl)-5-chlorobenzamide (0.7g, 1.2 mmol) reacted with methanesulfonyl chloride (0.1 mL, 1.3 mmol) to afford *N*-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-(methylsulfonyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(4-methylpiperazin-1-yl)-5-chlorobenzamide. Purification by HPLC on a C18 Dynamax column with 20-80% acetonitrile in water gradient with 0.1% trifluoroacetic acid afforded the trifluoroacetic acid salt as a white solid; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.5 (s, 1), 8.4 (d, 1), 8.2 (d, 1), 7.9 (dd, 1), 7.8 (s, 1), 7.4 (d, 2), 4.3 (s, 2), 3.4 (d, 2), 3.0 (s, 2), 2.9 (s, 3), 2.7 (s, 3), 2.4 (br s, 3), 2.2 (s, 4) ppm.

D. In a similar manner, the following compounds were made:

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-(methylsulfonyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(morpholin-4-yl)-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 9.8 (s, 1), 7.3-8.7 (m, 6), 3.9 (s, 2), 4.3 (s, 2), 3.8-4.0 (m, 4), 2.8-3.0 (m, 4), 2.9 (s, 3) ppm.

E. Other compounds of the invention may be prepared by methods similar to those described in this Example and by methods known to those of ordinary skill in the art.

EXAMPLE 5

Compounds of Formula (Ig)

A. To a solution of *N*-(5-chloropyridin-2-yl)-2-[((4-((methylamino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide (1.0 g, 2.0 mmol) in dioxane (20 mL) was added ethyl isocyanate (0.18 mL, 2.2 mmol) and the reaction stirred at ambient temperature. After 16 hours, the mixture was concentrated of all volatiles *in vacuo*. The residual solid was purified by flash chromatography on silica gel to afford 0.85 g (74% yield) of *N*-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N''*-ethylureido)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, as a white solid; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.4 (s, 1), 8.4 (s, 1), 8.1 (d, 1), 7.9 (d, 1), 7.5 (s, 1), 7.4 (s, 1), 7.3 (s, 1), 4.4 (s, 2), 3.9 (s, 3), 3.1 (q, 2), 2.8 (s, 3), 1.0 (t, 3) ppm.

B. In a similar manner, the following compounds were made:

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N''*-ethylureido)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(4-(*tert*-butoxycarbonyl)piperazin-1-yl)-5-chlorobenzamide; NMR (DMSO-d_6) 10.9 (s, 1), 9.5 (s, 1), 8.3 (d, 1), 8.1 (d, 1), 7.9 (dd, 1), 7.5 (s, 1), 7.4 (s, 1), 7.3 (s, 1), 6.4 (t, 1), 4.3 (s, 2), 3.3 (m, 4), 3.1 (m, 2), 2.9 (m, 4), 2.8 (s, 3), 1.4 (s, 9), 1.0 (t, 3) ppm.

C. In a manner similar to that described in Paragraph A above, *N*-(5-chloropyridin-2-yl)-2-[((4-((methylamino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide (1.0 g, 2.0 mmol) reacted with morpholinoethyl isothiocyanate (0.34 g, 2.0 mmol) in THF (20 mL) to afford *N*-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N''*-(2-(morpholin-4-yl)ethyl)thioureido)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide. Purification by HPLC on a C18 Dynamax column with acetonitrile in water gradient with 0.1% trifluoroacetic acid afforded the trifluoroacetic acid salt as a white solid; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.7 (br s, 1), 9.3 (s, 1), 7.2-8.3 (m, 7), 4.9 (s, 2), 3.9 (t, 4), 3.8 (s, 3), 3.7 (t, 2), 3.5 (d, 2), 3.3 (br, 2), 3.2 (br, 5) ppm.

D. In a similar manner, the following compounds were made:

N-(5-chloropyridin-2-yl)-2-[((4-((*N''*-methyl-*N'*-(2-(pyrrolidin-1-yl)ethyl)ureido)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(morpholin-4-yl)-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.9 (d, 1), 9.6 (d, 1), 7.3-8.5 (m, 6), 2.9-4.5 (m, 12), 2.8 (s, 3), 2.4 (br d, 2), 1.7-2.0 (m, 4) ppm.

E. A solution of potassium cyanate (0.70g, 8.6 mmol) in methanol (4 mL) was added dropwise to a solution of *N*-(5-chloropyridin-2-yl)-2-[((4-((methylamino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide (0.10 g, 0.20 mmol) in acetic acid (1.5 mL), and the mixture was stirred at ambient temperature for 20 hours. Concentration and purification by HPLC on a C18 Dynamax column with 20-70% acetonitrile in water gradient with 0.1% trifluoroacetic acid afforded *N*-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methylureido)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt as a white solid; NMR (DMSO-d_6/TFA) 10.9 (br s, 1), 9.3 (s, 1), 8.2 (s, 1), 8.1 (s, 1), 7.8 (d, 1), 7.5 (s, 1), 7.2 (s, 2), 4.4 (s, 2), 3.8 (s, 3), 2.9 (s, 3) ppm.

F. In a similar manner, the following compounds were made:

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-(2-hydroxyethyl)ureido)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide; NMR ($CDCl_3$) 9.7 (br s, 1), 9.0 (s, 1), 8.3 (d, 1), 8.0 (d, 1), 7.7 (dd, 1), 7.4 (s, 1), 7.2 (d, 1), 7.0 (s, 1), 5.8 (br s, 2), 4.4 (s, 2), 3.9 (s, 3), 3.8 (br s, 1), 3.7 (t, 2), 3.4 (t, 2) ppm.

G. To a solution of bis(trichloromethyl) carbonate (0.15 g, 0.51 mmol) in CH_2Cl_2 (5 mL) at 0°C was added *N*-(5-chloropyridin-2-yl)-2-[((4-((methylamino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide (0.10 g, 0.20 mmol), and the mixture stirred for 0.5 hour. Ethanolamine (0.40 mL, 6.6 mmol) was then added and the mixture was stirred at ambient temperature for 4 hours. Concentration *in vacuo* and purification by HPLC on a C18 Dynamax column with 20-70% acetonitrile in water gradient with

0.1% trifluoroacetic acid afforded *N*-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N"*-(2-hydroxyethyl)ureido)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt as a white solid; NMR (DMSO-d_6/TFA) 10.9 (br s, 1), 9.3 (s, 1), 8.3 (d, 1), 8.1 (d, 1), 7.8 (dd, 1), 7.7 (br s, 1), 7.5 (s, 1), 7.3 (s, 1), 7.2 (s, 1), 4.4 (s, 2), 3.8 (s, 3), 3.4 (t, 2), 3.1 (t, 2), 2.8 (s, 3) ppm.

H. In a similar manner, the following compounds were made:

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-((4-(2-hydroxyethyl)piperazin-1-yl)carbonyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.7 (s, 1), 9.3 (s, 1), 7.2-8.3 (m, 6), 4.3 (s, 2), 3.9 (s, 3), 3.0-3.7 (m, 12), 2.7 (s, 3) ppm.

I. To a solution of *N*-(5-chloropyridin-2-yl)-2-[((4-((methylamino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide (0.42 g, 0.87 mmol) in dioxane (5 mL) was added ethyl 3-isocyanatopropionate (0.15 mL, 1.0 mmol) and the mixture stirred at ambient temperature. After 0.5 hours, water (2 mL) was added resulting in a heterogeneous mixture. LiOH·H_2O (large excess) was added and the mixture stirred for 2 hours, then concentrated *in vacuo*. Purification by HPLC on a C18 Dynamax column with acetonitrile in water gradient with 0.1% trifluoroacetic acid afforded *N*-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N"*-(2-carboxyethyl)ureido)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt, as a white solid: NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.4 (s, 1), 8.3 (s, 1), 8.1 (d, 1), 7.9 (d, 1), 7.5 (s, 1), 7.4 (s, 1), 7.3 (s, 1), 4.3 (s, 2), 3.9 (s, 3), 3.3 (t, 2), 2.8 (s, 3), 2.4 (t, 2) ppm.

J. Other compounds of the invention may be prepared by methods similar to those described in this Example and by methods known to those of ordinary skill in the art.

EXAMPLE 6

Compounds of Formula (Ij)

A. To a solution of *N*-(5-chloropyridin-2-yl)-2-[((4-((methylamino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide (1.6 g, 3.2 mmol) and diisopropylethylamine (1.7 mL, 9.6 mmol) in CH_2Cl_2 (10 mL) at 0°C was added 2-chloroacetyl chloride (0.25 mL, 3.2 mmol). The mixture was stirred and allowed to warm to ambient temperature. After 7 hours, 4-hydroxypiperidine (0.65 g, 6.4 mmol) was added and the reaction stirred for 16 hours. The mixture was concentrated of all volatiles *in vacuo* and the resulting oil purified by HPLC on a C18 Dynamax column with acetonitrile in water gradient with 0.1% trifluoroacetic acid to afford *N*-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-(((4-

hydroxypiperidin-1-yl)methyl)carbonyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt as a white solid; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.5 (br s, 1), 9.4 (s, 1), 8.4 (s, 1), 8.1 (d, 1), 7.9 (d, 1), 7.7 (s, 1), 7.4 (s, 1), 7.3 (s, 1), 4.5 (m, 2), 4.3 (m, 2), 3.9 (m, 1), 3.9 (s, 3), 3.6 (m, 1), 3.4 (m, 1), 3.2 (m, 2), 3.0 (s, 3), 2.0 (m, 2), 1.7 (m, 2) ppm.

B. To a solution of *N*-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-((2-chloroethyl)sulfonyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide (1.1 g, 1.8 mmol) in DMF (5 mL) was added Cs_2CO_3 (5.7 g, 18 mmol), followed by 4-hydroxypiperidine (0.27 g, 2.6 mmol). The mixture was stirred at ambient temperature for 16 hours, then filtered and concentrated *in vacuo*. Purification of the resulting oil by flash chromatography on silica gel afforded 1.0g (82% yield) of *N*-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-((2-(4-hydroxypiperidin-1-yl)ethyl)sulfonyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, as a white solid; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.5 (br s, 1), 9.4 (s, 1), 8.4 (s, 1), 8.1 (d, 1), 7.9 (d, 1), 7.8 (s, 1), 7.4 (s, 1), 7.3 (s, 1), 4.3 (s, 2), 3.9 (m, 1), 3.9 (s, 3), 3.7 (m, 2), 3.5 (m, 2), 3.3 (m, 2), 3.2 (m, 1), 3.0 (m, 1), 2.8 (m, 3), 2.0 (m, 1), 1.8 (m, 2), 1.6 (m, 1) ppm.

C. In a similar manner, the following compounds were made:

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-((2-(pyrrolidin-1-yl)ethyl)sulfonyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.4 (s, 1), 8.3 (s, 1), 8.1 (d, 1), 7.9 (d, 1), 7.8 (s, 1), 7.4 (s, 1), 7.3 (s, 1), 4.4 (s, 2), 3.9 (s, 3), 3.6 (m, 6), 3.1 (br m, 2), 2.8 (s, 3), 2.1 (m, 2), 1.9 (m, 2) ppm.

D. Other compounds of the invention may be prepared by methods similar to those described in this Example and by methods known to those of ordinary skill in the art.

EXAMPLE 7

Compounds of Formula (Ik)

A. To a solution of *N*-(5-chloropyridin-2-yl)-2-[((4-((methylamino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide (0.10 g, 0.20 mmol) in DMF (3 mL) were added triethylamine (0.28 mL, 2.0 mmol) and 1*H*-pyrazole-1-carboxamidine hydrochloride (0.30 g, 2.0 mmol). The mixture was stirred at ambient temperature for 15 hours, then heated at 45°C for 3 hours. The cooled mixture was acidified with trifluoroacetic acid and purified by HPLC on a C18 Dynamax column with 20-70% acetonitrile in water gradient with 0.1% trifluoroacetic acid to afford *N*-(5-chloropyridin-2-yl)-2-[((4-(((amidino)(methyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt as white solid; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.4

(s, 1), 8.3 (d, 1), 8.1 (d, 1), 7.8 (dd, 1), 7.6 (s, 1), 7.4 (br s, 4), 7.3 (s, 1), 7.2 (s, 1), 4.5 (s, 2), 3.8 (s, 3), 2.9 (s, 3) ppm.

B. Other compounds of the invention may be prepared by methods similar to those described in this Example and by methods known to those of ordinary skill in the art.

EXAMPLE 8

Compounds of Formula (Im)

A. To a solution of *N*-(5-chloropyridin-2-yl)-2-[((4-((methylamino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide (0.70 g, 1.4 mmol) in MeOH (30 mL) was added triethylamine (3 mL, 22 mmol) and ethyl acetimidate hydrochloride (large excess). The reaction was stirred at ambient temperature for 16 hours, then concentrated of all volatiles *in vacuo*. Purification of the residual oil by HPLC on a C18 Dynamax column with acetonitrile in water gradient with 0.1% trifluoroacetic acid afforded *N*-(5-chloropyridin-2-yl)-2-[((4-((*N*'-(1-iminoethyl)-*N*'-methylamino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt as a white solid; NMR (DMSO-d_6/TFA) (rotational isomers observed) 10.9 (s, 1), 9.4 (s, 1), 9.3 (br s, 1), 8.6 (br s, 1), 8.4 (s, 1), 8.1 (d, 1), 7.9 (d, 1), 7.8 (s, 1), 7.4 (s, 1), 7.3 (s, 1), 4.6 (s, 2), 3.9 (s, 3), 3.1 (s, 3), 2.3 (s, 3) ppm.

B. To a solution of *N*-(5-chloropyridin-2-yl)-2-[((4-((methylamino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide (3.0 g, 6.0 mmol) in DMF (30 mL) were added *N,N*-diisopropylethylamine (1.94 g, 15 mmol) and 2-methylthioimidazoline hydroiodide (1.9 g, 7.8 mmol). The mixture was heated at 90°C for 20 hours. The cooled mixture was poured into water, extracted with ethyl acetate, dried ($MgSO_4$) and concentrated *in vacuo*. Purification by HPLC on a C18 Dynamax column with 20-70% acetonitrile in water gradient with 0.1% trifluoroacetic acid afforded *N*-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(3,4-dihydro-2*H*-pyrrol-5-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt, as white solid; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.7 (d, 1), 9.4 (d, 1), 8.3 (m, 1), 8.2 (d, 1), 8.1 (d, 1), 7.8 (d, 1), 7.7 (d, 1), 7.3 (d, 1), 7.2 (d, 1), 4.6 (d, 2), 3.9 (s, 3), 3.6 (m, 2), 2.9~3.2 (m, 5), 2.2 (m, 2) ppm.

C. Sodium hydride (60%, 0.1 g, 2.5 mmol) was added in portions to a mixture of ethyl (2-trifluoroethyl)acetimidate hydrochloride (0.53 g, 2.5 mmol) and DMF (4 mL), and stirred at 0°C for 5 minutes, then at ambient temperature for 20 minutes. The mixture was re-cooled to 0°C, and *N*-(5-chloropyridin-2-yl)-2-[((4-((methylamino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide (0.25 g, 0.5 mmol) was added. After stirring

at ambient temperature for 15 hours, cesium carbonate (0.6 g, 1.8 mmol) was added and the stirring was continued for 5 days. The mixture was cooled in an ice bath, and trifluoroacetic acid (0.5 mL) was added dropwise. Purification by HPLC on a C18 Dynamax column with 20-70% acetonitrile in water gradient with 0.1% trifluoroacetic acid gave 0.15g of *N*-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-(1-imino-4,4,4-trifluorobutyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt, as a white solid; NMR (DMSO-d_6/TFA) 10.90 (s, 1), 9.3-9.4 (m, 2), 8.90 (d, 1), 8.30 (m, 1), 8.10 (d, 1), 7.75-7.85 (m, 2), 7.30 (s, 1), 7.25 (s, 1), 4.70 (s, 0.8), 4.60 (s, 1.2), 3.80 (s, 1), 3.20 (s, 1.8), 3.00 (s, 1.2), 2.90 (m, 2), 2.60 (m, 2) ppm.

D. In a similar manner, the following compounds were made:

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-ethyl-*N'*-(3-cyano-1-iminopropyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6) 10.90 (s, 1H), 9.90 (s, 1H), 9.70 (s, 1H), 9.40 (s, 1H), 8.40 (d, 1H), 8.10 (d, 1H), 7.90 (dd, 1H), 7.80 (s, 1H), 7.40 (d, 1H), 7.25 (d, 1H), 4.80 (s, 2H), 3.90 (s, 3H), 3.55 (q, 2H), 3.20-3.10 (m, 2H), 3.00-2.90 (m, 2H), 1.20 (t, 3H) ppm; and

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-(1-imino-4,4,4-trifluorobutyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.85 (s, 1), 9.90 (b, 1), 9.40 (b, 1), 9.35 (s, 1), 9.00 (b, 1), 8.28 (d, 1), 8.08 (d, 1), 7.85 (s, 1), 7.80 (dd, 1), 7.25 (d, 1), 4.40 (d, 2), 3.80 (s, 3), 2.60-2.70 (m, 4) ppm.

E. Other compounds of the invention may be prepared by methods similar to those described in this Example and by methods known to those of ordinary skill in the art.

EXAMPLE 9

Compounds of Formula (Io)

A. To a solution of *N*-(5-chloropyridin-2-yl)-2-[((4-((methylamino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-5-chlorobenzamide (1.0 g, 2.1 mmol) in THF (30 mL) at 0°C was added 2-bromoethylisocyanate (0.24 mL, 2.6 mmol) and the mixture stirred at ambient temperature. After 7 hours, an additional 0.12 mL (1.3 mmol) of 2-bromoethylisocyanate was added. After a further 16 h, the mixture was cooled to 0°C and triethylamine (0.60 mL, 4.3 mmol) was added. The reaction mixture was warmed slowly to ambient temperature and stirred for 24 hours, then concentrated of all volatiles *in vacuo*. The resulting gum was dissolved in ethyl acetate (50 mL), washed with brine (50 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash chromatography on silica gel afforded 0.77 g (67%) of *N*-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-(oxazolin-2-yl)amino)methyl)-3-

chlorothiophen-2-yl)carbonyl)amino]-5-chlorobenzamide; as a white foam; NMR ($CDCl_3$) 11.2 (s, 1), 8.7 (s, 1), 8.6 (d, 1), 7.4-8.3 (m, 6), 4.4 (s, 2), 4.4 (t, 2), 3.8 (t, 2), 3.0 (s, 3) ppm.

B. In a similar manner, the following compounds were made:

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(thiazolin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide; NMR (DMSO-d_6/TFA) 11.0 (s, 1), 10.1 (br d, 1), 9.5 (s, 1), 7.3-8.5 (m, 6), 4.7 (m, 2), 4 (m, 2), 3.9 (s, 3), 3.6 (m, 2), 3.2 (s, 3) ppm;

N-(4-chlorophenyl)-2-[((4-((*N*'-methyl-*N*'-(oxazolin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide; NMR (DMSO-d_6) 10.5 (s, 1), 10.3 (m, 1), 9.4 (s, 1), 7.3-8.0 (m, 7), 4.8 (m, 2), 4.6 (s, 2), 3.9 (m, 2), 3.8 (s, 3), 3.0 (s, 3) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-oxazolin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 10.3 (d, 1), 9.4 (s, 1), 7.3-8.4 (m, 6), 4.8 (t, 2), 4.5 (s, 2), 3.9 (t, 2), 3.8 (s, 3), 3.0 (s, 3) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-ethyl-*N*'-(dihydro-4(*H*)-1,3-oxazin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide; NMR (DMSO-d_6) 10.9 (s, 1), 9.4 (s, 1), 9.3 (br s, 1), 8.4 (s, 1), 8.1 (d, 1), 7.9 (d, 1), 7.8 (s, 1), 7.4 (s, 1), 7.3 (s, 1), 4.6 (m, 2), 4.5 (s, 2), 3.9 (s, 3), 3.4 (m, 4), 2.0 (m, 2), 1.1 (t, 3) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-ethyl-*N*'-(oxazolin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide; NMR ($CDCl_3$) 9.0 (s, 1), 8.9 (s, 1), 8.2 (d, 1), 8.1 (d, 1), 7.6 (dd, 1), 7.4 (s, 1), 7.3 (d, 1), 7.0 (d, 1), 4.4 (s, 2), 4.3 (t, 2), 3.9 (s, 3), 3.8 (t, 2), 3.3 (q, 2), 1.1 (t, 3) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-(2,2,2-trifluoroethyl)-*N*'-(oxazolin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.4 (s, 1), 8.3 (d, 1), 8.1 (d, 1), 7.8 (d, 1), 7.75 (d, 1), 7.2 (d, 2), 4.9 (t, 2), 4.7 (s, 2), 4.4 (br s, 2), 3.9 (t, 2), 3.8 (s, 3) ppm.

C. In a similar manner to that described in Paragraph A above, *N*-(5-chloropyridin-2-yl)-2-[((4-((methylamino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide (1.5 g, 3.0 mmol) reacted with 3-bromopropylisocyanate (0.54 mL, 3.6 mmol), followed by triethylamine (2.0 mL, 15 mmol) to afford *N*-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(dihydro-4(*H*)-1,3-oxazin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide. Purification by HPLC on a C18 Dynamax column with acetonitrile in water gradient with 0.1% trifluoroacetic acid afforded the trifluoroacetic acid salt as a white

solid; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.4 (s, 1), 9.3 (br s, 1), 8.4 (s, 1), 8.1 (d, 1), 7.9 (d, 1), 7.9 (s, 1), 7.4 (s, 1), 7.3 (s, 1), 4.6 (m, 2), 4.5 (s, 2), 3.9 (s, 3), 3.4 (m, 2), 3.0 (s, 3), 2.0 (s, 2) ppm.

D. In a similar manner, the following compounds were made:

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(oxazolin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(morpholin-4-yl)-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 10.3 (d, 1), 9.4 (s, 1), 7.2-8.4 (m, 6), 4.8 (t, 2), 4.6 (s, 2), 3.9 (t, 2), 3.8 (s, 3), 3.7 (br d, 4), 3.0 (s, 3), 2.9 (br d, 4) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-ethyl-*N*'-(thiazolin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 10.1 (br d, 1), 9.4 (d, 1), 7.2-8.4 (m, 6), 4.7 (d, 2), 4.0 (q, 2), 3.9 (s, 3), 3.4-3.7 (m, 4), 1.0-1.2 (m, 3) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(4-(oxo)oxazolin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 10.5 (s, 1), 9.4 (d, 1), 7.3-8.4 (m, 6), 4.5-4.8 (m, 4), 3.9 (s, 3), 3.4-3.7 (m, 4), 3.0 (d, 3) ppm;

N-(4-chlorophenyl)-2-[((4-((*N*'-methyl-*N*'-(oxazolin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(morpholin-4-yl)-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.5 (s, 1), 10.3 (d, 1), 9.6 (s, 1), 7.3-8.1 (m, 7), 4.9 (t, 2), 4.6 (s, 2), 3.9 (t, 2), 3.7 (br d, 4), 3.0 (s, 3), 2.9 (br d, 4) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-ethyl-*N*'-(oxazolin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(morpholin-4-yl)-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 10.3 (s, 1), 9.5 (s, 1), 7.3-8.1 (m, 6), 4.9 (m, 2), 4.6 (s, 2), 3.9 (m, 2), 3.7 (m, 4), 3.4 (m, 2), 2.9 (m, 4), 1.0 (m, 3) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-(*t*-butyl)-*N*'-(oxazolin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.4 (s, 1), 8.4 (d, 1), 8.1 (d, 1), 7.9 (dd, 1), 7.5 (s, 1), 7.4 (d, 1), 7.2 (d, 1), 4.4 (s, 2), 4.1 (t, 2), 3.9 (s, 3), 3.6 (t, 2), 1.4 (s, 9) ppm;

5-(*N*-(5-chloropyridin-2-yl)amino)carbonyl-6-[4-((*N*'-methyl-*N*'-(oxazolin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl]amino-1,3-benzodioxole, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.4 (s, 1), 10.0 (s, 1), 9.2 (s, 1), 6.5-7.4 (m, 6), 5.2 (s, 2), 3.8 (t, 2), 3.6 (s, 2), 2.8 (t, 2), 2.0 (s, 3) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-(2-methoxyethyl)-*N*'-(oxazolin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 11.0 (s, 1), 10.3 (d, 1), 9.4 (s, 1), 7.2-8.4(m, 6), 4.8 (m, 2),

4.6 (s, 2), 3.9 (s, 6), 3.5 (s, 2), 3.4 (s, 2), 3.2 (d, 2) ppm;

5-(*N*-(5-chloropyridin-2-yl)amino)carbonyl-6-[4-((*N'*-(2-methoxyethyl)-*N'*-(oxazolin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl]amino-1,3-benzodioxole, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 11.5 (d, 1), 11.0 (s, 1), 10.3 (d, 1), 7.5-8.4 (m, 6), 6.1 (s, 2), 4.8 (s, 2), 4.6 (s, 2), 3.9 (m, 3), 3.4-3.6 (m, 4), 3.2 (d, 2) ppm.

E. Other compounds of the invention may be prepared by methods similar to those described in this Example and by methods known to those of ordinary skill in the art.

EXAMPLE 10

Compounds of Formula (Iq)

A. A mixture of *N*-(5-chloropyridin-2-yl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-hydroxy-5-chlorobenzamide (2.1g, 3.7 mmol) and cesium carbonate (8 g, 25 mmol) in dimethyl formamide (50 mL) was stirred at ambient temperature for 1.0 hour. A solution of 1-chloro-3-iodopropane (1.1 g, 5.6 mmol) in dimethyl formamide (1.5 mL) was added dropwise, and stirring continued for 18 hours. 2-(methylamino)ethanol (1.5 mL, 18.7 mmol) was then added, and the mixture was heated at 65°C for 12 hours. After cooling to ambient temperature the mixture was filtered, and the filtrate was acidified with trifluoroacetic acid. Purification by HPLC on a C18 Dynamax column with 20-70% acetonitrile in water gradient with 0.1% trifluoroacetic acid afforded *N*-(5-chloropyridin-2-yl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(3-(*N'*-methyl-*N'*-(2-hydroxyethyl)amino)propoxy)-5-chlorobenzamide, trifluoroacetic acid salt as tan solid; NMR (DMSO-d_6/TFA) 11.0 (s, 1), 9.6 (s, 1), 9.4 (br, m, 1), 8.3 (s, 1), 8.2 (s, 1), 8.1 (d, 1), 7.8 (d, 1), 7.4 (s, 1), 7.3 (s, 1), 4.4 (s, 2), 4.2 (br t, 2), 3.0-4.0 (m, 14), 2.9 (s, 3), 2.8 (s, 3), 2.1 (m, 2) ppm.

B. In a similar manner, the following compounds were made:

N-(5-chloropyridin-2-yl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(3-morpholinylpropoxy)-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 11.0 (s, 1), 9.9 (br s, 1), 9.6 (s, 1), 8.4 (d, 10), 8.2 (s, 1), 8.1 (d, 1), 7.9 (dd, 1), 7.4 (s, 1), 7.3 (s, 1), 4.4 (s, 2), 4.2 (t, 2), 3.9 (d, 2), 3.3-3.8 (m, 12), 3.3 (t, 2), 2.9-3.1 (m, 2), 2.9 (s, 3), 2.1 (m, 2) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(3-(pyrrolidin-1-yl)propoxy)-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 11.0 (s, 1), 9.6 (s, 1), 8.4 (d, 1), 8.2 (s, 1), 8.15 (d, 1), 7.9 (dd, 1), 7.4 (s, 1), 7.3 (s, 1), 4.4 (s, 2), 4.2 (t, 2), 3.2-3.8 (m, 12), 3.0 (m, 2), 2.9 (s, 3), 2.1 (m, 2), 1.9 (m, 2), 1.8 (m, 2) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(1-methylpiperidin-4-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(3-(morpholin-4-yl)propoxy)-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 11.0 (s, 1), 9.9 (br s, 1), 9.8 (br m, 1), 9.6 (s, 1), 8.4 (d, 1), 8.2(s, 1), 8.1 (d, 1), 7.8 (dd, 1), 7.4 (s, 1), 7.3 (s, 1), 4.4 (br m, 2), 4.2 (t, 2), 3.9 (d, 2), 3.5-3.7 (m, 5), 3.4 (d, 2), 3.3 (t, 2), 3.0 (m, 4), 2.8 (s, 3), 2.7 (s, 3), 2.3 (m, 2), 2.1 (m, 2), 2.0 (br q, 2) ppm;

N-(4-chlorophenyl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(3-(morpholin-4-yl)propoxy)-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.6 (s, 1), 9.9 (br m, 1), 9.7 (s, 1), 8.2 (s, 1), 7.7 (d, 2), 7.4 (s, 1), 7.4 (s, 1), 7.3 (d, 2), 4.4 (s, 2), 4.2 (br t, 2), 3.9 (d, 2), 3.0-3.7 (m, 16), 2.9 (s, 3), 2.1(m, 2) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(2-hydroxyethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(3-(pyrrolidin-1-yl)propoxy)-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 11.0 (s, 1), 9.7 (br s, 2), 9.6 (s, 1), 8.3 (d, 1), 8.2(s, 1), 8.1 (d, 1), 7.8 (dd, 1), 7.4 (s, 1), 7.3 (s, 1), 4.3 (br d, 2), 4.2 (t, 2), 3.7 (t, 2), 3.5 (m, 2), 3.3 (m, 2), 3.2 (m, 2), 2.9 (m, 2), 2.7 (s, 3), 2.1 (m, 2), 1.9 (m, 2), 1.8 (m, 2) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(2-hydroxyethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(3-(morpholin-4-yl)propoxy)-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 11.0 (s, 1), 9.8 (br s, 1), 9.7 (br s, 1), 9.6 (s, 1), 8.3 (d, 1), 8.2 (s, 1), 8.1 (d, 1), 7.8 (dd, 1), 7.4 (s, 1), 7.3 (s, 1), 4.3 (br d, 2), 4.2 (t, 2), 3.9 (d, 2), 3.7 (t, 2), 3.6 (t, 2), 3.4 (d, 2), 3.3 (m, 2), 3.2 (m, 2), 3.0 (m, 2), 2.7 (s, 3), 2.1 (m, 2) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(3-(imidazol-1-yl)propoxy)-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 11.0 (s, 1), 9.7 (s, 1), 9.0 (s, 1), 8.4 (d, 1), 8.2 (s, 1), 8.1 (d, 1), 7.9 (dd, 1), 7.7(s, 1), 7.6 (s, 1), 7.3 (s, 2), 4.4 (br m, 4), 4.0 (t, 2), 3.1-3.7 (m, 8), 2.8 (s, 3), 2.2 (m, 2) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(2-hydroxyethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(3-(imidazol-1-yl)propoxy)-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 11.0 (s, 1), 10.7 (s, 1), 9.1 (s, 1), 8.3 (d, 1), 8.2 (s, 1), 8.1(d, 1), 7.8 (dd, 1), 7.7 (s, 1), 7.6 (s, 1), 7.3 (s, 2), 4.2-4.5 (m, 4), 4.0 (t, 2), 3.8 (t, 2), 3.2 (m, 2), 2.8 (s, 3), 2.2 (m, 2) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(methylsulfonyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(3-(4-ethylpiperazin-1-yl)propoxy)-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 11.0 (br s, 1), 9.5 (s, 1), 8.3 (d, 1), 8.1

(d, 1), 7.9 (dd, 1), 7.8 (s, 1), 7.4 (s, 1), 7.3 (s, 1), 4.2 (br s, 2), 3.1-3.9 (m, 10), 2.9 (s, 3), 2.7 (s, 3), 2.2 (m, 2), 1.2 (t, 3) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(2-hydroxyethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(3-(pyridin-3-yloxy)propoxy)-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6) 11.0 (s, 1), 9.6 (s, 1), 7.9-8.7 (m, 8), 7.4 (d, 2), 4.4 (m, 6), 3.9 (m, 2), 2.8 (s, 3), 2.2 (m, 2) ppm.

C. To a solution of *N*-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(2-(pyrrolidin-1-yl)ethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-hydroxy-5-chlorobenzamide (1.3 g, 1.7 mmol) in DMF (30 mL) was added sodium hydride (60% dispersion in mineral oil, 0.16 g, 4.0 mmol), followed after 0.5 hour by 2-bromoethyl acetate (0.37 g, 2.2 mmol). The mixture was stirred at ambient temperature. After 24 hours NaOH (25% solution in water, 3 mL) was added, and the mixture was stirred for a further 4 hours. The mixture was acidified with trifluoroacetic acid, and purified by HPLC on a C18 Dynamax column with 20-70% acetonitrile in water gradient with 0.1% trifluoroacetic acid to afford *N*-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(2-(pyrrolidin-1-yl)ethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2-hydroxyethoxy)-5-chlorobenzamide, trifluoroacetic acid salt as white solid; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.6 (s, 1), 8.3 (d, 1), 8.2 (s, 1), 8.1 (d, 1), 7.8 (dd, 1), 7.4 (s, 1), 7.3 (s, 1), 4.4 (s, 2), 4.2 (t, 2), 3.7 (t, 2), 3.6 (m, 2), 3.5 (m, 2), 3.0-3.8 (br m, 4), 2.8 (s, 3), 2.0 (br s, 4) ppm. Also obtained from this reaction was *N*-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(2-(pyrrolidin-1-yl)ethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2-acetoxyethoxy)-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.8 (s, 1), 9.4 (s, 1), 8.3 (s, 1), 8.2 (s, 1), 8.1 (d, 1), 7.8 (d, 1), 7.4 (s, 1), 7.3 (s, 1), 4.4 (s, 2), 4.3 (s, 4), 3.6 (m, 4), 3.5 (m, 4), 3.1-3.6 (br m, 4), 2.8 (s, 3), 1.9 (s, 3) ppm.

D. In a similar manner, the following compounds were made:

N-(5-chloropyridin-2-yl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2-hydroxyethoxy)-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.6 (s, 1), 8.3 (d, 1), 8.2 (s, 1), 8.1 (d, 10), 7.8 (dd, 1), 7.4 (s, 1), 7.3 (s, 1), 4.4 (s, 2), 4.2 (t, 2), 3.7 (t, 2), 3.1-3.9 (br m, 8), 2.8 (s, 3) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(2-(dimethylamino)ethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2-hydroxyethoxy)-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.6 (s, 1), 8.3 (d, 1), 8.2 (s, 1), 8.1 (d, 1), 7.8 (dd, 1), 7.3 (s, 1), 7.2 (s, 1), 4.4 (s, 2), 4.1 (t, 2), 3.7 (t, 2), 3.5 (br s, 4), 2.9 (s, 6), 2.8 (s, 3) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(1-methylpiperidin-4-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2-hydroxyethoxy)-5-chlorobenzamide,

trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 11.0 (s, 1), 9.6 (s, 1), 8.4 (s, 1), 8.2 (s, 1), 8.1 (d, 1), 7.9 (dd, 1), 7.4 (s, 1), 7.3 (s, 1), 4.4 (br, 4), 4.2 (t, 2), 3.9-3.3 (m, 6), 3.2 (s, 3), 2.9 (s, 3), 2.4-2.2 (m, 4) ppm.

E. Other compounds of the invention may be prepared by methods similar to those described in this Example and by methods known to those of ordinary skill in the art.

EXAMPLE 11

Compounds of Formula (Ir)

A. To a solution of *N*-(5-chloropyridin-2-yl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-hydroxy-5-chlorobenzamide (1.0 g, 1.8 mmol) in DMF (15 mL) was added sodium hydride (0.051 g, 2.2 mmol) and the mixture stirred at ambient temperature. After 0.5 hours, ethyl bromoacetate (0.30 g, 1.8 mmol) was added and stirring continued. After 3 hours, the mixture was cooled to 0°C and acidified with trifluoroacetic acid. Purification by HPLC on a C18 Vydac column with acetonitrile in water gradient with 0.1% trifluoroacetic acid afforded *N*-(5-chloropyridin-2-yl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(ethoxycarbonyl)methoxy-5-chlorobenzamide, trifluoroacetic acid salt as a white solid; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.4 (s, 1), 8.4 (dd, 1), 8.1 (d, 1), 8.0 (s, 1), 7.9 (dd, 1), 4.6 (s, 2), 4.3 (q, 2), 4.2 (s, 2), 3.8 (s, 4), 3.4 (s, 4), 3.4 (s, 3), 1.2 (t, 3) ppm.

B. In a similar manner, the following compounds were made:

N-(5-chloropyridin-2-yl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(methylthio)methoxy-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.8 (s, 1), 9.3 (s, 1), 8.3 (s, 1), 8.1 (d, 1), 8.1 (s, 1), 7.9 (dd, 1), 7.2 (s, 1), 7.12 (s, 1), 4.9 (s, 2), 4.3 (s, 2), 3.6 (s, 4), 3.5 (s, 4), 3.2 (s, 3), 2.4 (s, 3) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(2-(pyrrolidin-1-yl)ethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2-methoxyethoxy)-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.5 (s, 1), 8.4 (s, 1), 8.2 (s, 1), 8.1 (d, 1), 7.9 (br, 1), 7.2 (s, 1), 7.2 (s, 1), 4.4 (s, 2), 4.2 (br, 2), 3.7 (br, 2), 3.6 (br, 2), 3.5 (br, 2), 3.3 (s, 3), 2.8 (s, 3), 1.9 (br, 4) ppm;

N-(4-chlorophenyl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(ethoxycarbonyl)methoxy-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.6 (s, 1/2), 10.5 (s, 1), 9.3 (s, 1/2), 7.8 (s, 1), 7.6 (d, 2), 7.4 (d, 2), 7.2 (s, 1), 7.1 (s, 1), 4.6 (s, 2), 4.2 (q, 2), 3.6 (s, 2), 3.4 (br, 8), 3.2 (t, 3), 3.1 (s, 3) ppm;

N-(4-chlorophenyl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-

yl)carbonyl)amino]-3-((acetoxy)ethoxy)-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.4 (s, 1), 9.5 (s, 1), 7.7 (d, 2), 7.4 (s, 1), 7.2 (d, 2), 7.1 (s, 1), 4.4 (s, 2), 4.4 (s, 4), 3.5 (br, 8), 2.9 (s, 3), 1.9 (s, 1) ppm;

N-(4-chlorophenyl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2-(morpholin-4-yl)ethoxy)-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.6 (s, 1), 9.7 (s, 1), 8.2 (s, 1), 7.7 (d, 2), 7.5 (s, 1), 7.4 (s, 1), 7.2 (d, 2), 4.5 (s, 2), 4.4 (s, 2), 3.9-3.1 (m, 20), 2.9 (s, 3) ppm;

N-(4-chlorophenyl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-((methylthio)methoxy)-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.6 (s, 1), 9.6 (s, 1), 8.2 (s, 1), 7.7 (d, 2), 7.5 (s, 1), 7.3 (d, 2), 5.4 (s, 2), 4.4 (s, 2), 3.2 (br, 8), 3.9 (s, 3), 2.2 (s, 3) ppm.

C. To a solution of *N*-(5-chloropyridin-2-yl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-hydroxy-5-chlorobenzamide (2.0 g, 3.6 mmol) in DMF (20 mL) were added cesium carbonate (8.0g, 25 mmol) and 2-bromoethyl ethyl ether (0.71g, 4.6 mmol). The suspension was heated at 60°C for 16 hours. The mixture was cooled to ambient temperature and filtered, and the filtrate was acidified with trifluoroacetic acid. Purification by HPLC on a C18 Dynamax column acetonitrile in water gradient with 0.1% trifluoroacetic acid afforded *N*-(5-chloropyridin-2-yl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2-ethoxyethoxy)-5-chlorobenzamide, trifluoroacetic acid salt as a white solid; NMR (DMSO-d_6/TFA) 11.9 (s, 1), 9.4 (s, 1), 8.3 (d, 1), 8.2 (s, 1), 8.1 (d, 1), 7.9 (dd, 1), 7.4 (s, 1), 7.3 (s, 1), 4.4 (s, 2), 4.2 (t, 2), 3.7 (t, 2), 3.5 (q, 2), 3.5 (br, 8), 2.9 (s, 3), 1.0 (t, 3) ppm.

D. In a similar manner, the following compounds were made:

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(2-hydroxyethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2-methoxyethoxy)-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.6 (br s, 1), 9.4 (s, 1), 8.3 (d, 1), 8.2 (s, 1), 8.1 (d, 1), 7.8 (d, 1), 7.4 (s, 1), 7.3 (s, 1), 4.3 (br d, 2), 4.2 (t, 2), 3.7 (t, 2), 3.6 (m, 2), 3.3 (s, 3), 3.2 (m, 2), 2.8 (s, 3) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((4-ethylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2-(2-methoxyethoxy)ethoxy)-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.4 (s, 1), 8.3 (d, 1), 8.2 (s, 1), 8.1 (d, 1), 7.8 (dd, 1), 7.4 (s, 1), 7.2 (s, 1) , 4.5 (s, 2), 4.0 (t, 2), 3.0-3.8 (m, 16), 3.2 (s, 3), 1.2 (t, 3) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(methylsulfonyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2-aminoethoxy)-5-chlorobenzamide, trifluoroacetic acid salt;

NMR (DMSO-d_6/TFA) 11.0 (s, 1), 9.6 (s, 1), 8.3 (d, 1), 8.1 (d, 1), 7.9 (br s, 3), 7.8 (dd, 1), 7.8 (s, 1), 7.4 (d, 1), 7.3 (s, 1), 4.3 (t, 2), 4.2 (s, 2), 3.2 (m, 2) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(oxazolin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-((2-(2-methoxyethoxy)ethoxy)-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.8 (br, 1), 10.3 (br, 1), 9.4 (br, 1), 8.3 (s, 1), 8.1 (d, 1), 7.9 (d, 1), 7.8 (d, 1), 7.4 (s, 1), 7.3 (s, 1), 4.8 -4.4 (m, 3), 4.2 (m, 2), 3.9 (m, 2), 3.7 (m, 2), 3.5 (m, 2), 3.4 (m, 2), 3.2 (s, 3), 3.0 (s, 2), 2.8 (s, 2) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(methylsulfonyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2-(pyrrolidin-1-yl)ethoxy)-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 11.0 (br s, 1), 9.6 (br s, 2), 8.3(d, 1), 8.1 (d, 1), 7.8 (dd, 1), 7.7 (s, 1), 7.4 (s, 1), 7.3 (s, 1), 4.4 (m, 2), 4.2 (s,), 3.6 (m, 4), 3.1 (m,), 2.9 (s, 3), 2.7 (s, 3), 1.9 (m, 2), 1.8 (m, 2) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(2-hydroxyethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2-(imidazol-1-yl)ethoxy)-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 11.0 (s, 1), 9.6 (br s, 1), 9.5 (s, 1), 9.0 (s, 1), 8.3 (d, 1), 8.2 (s, 1), 8.1 (d, 1), 7.8 (dd, 1), 7.7 (s, 1), 7.5 (s, 1), 7.4 (s, 1), 7.3 (s, 1), 4.6 (m, 4), 4.4 (m, 1), 4.3 (m, 1), 3.8 (t, 2), 3.2 (m, 2), 2.8 (s, 3) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(methylsulfonyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2-(imidazol-1-yl)ethoxy)-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 10.4 (s, 1), 9.0 (s, 1), 8.3 (d, 1), 8.1 (d, 1), 7.9 (dd, 1), 7.8 (s, 1), 7.7 (s, 1), 7.5 (s, 1), 7.4 (s, 1), 7.3 (d, 1), 4.6 (br, 4), 4.2 (s, 2), 2.9 (s, 3), 2.6 (s, 3) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(2-hydroxyethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2-(pyrrolidin-1-yl)ethoxy)-5-chlorobenzamide; trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 11.0 (s, 1), 9.6 (s, 1), 8.4 (s, 1), 8.2 (s, 1), 8.1 (d, 1), 7.9 (dd, 1), 7.4 (s, 1), 7.4 (s, 1), 4.6 (s, 2), 4.9-3.6 (m, 8), 3.2 (dd, 4), 2.8 (s, 3), 2.0 (s, 3), 1.9 (br, 4) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(2,3-dihydroxypropyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2-methoxyethoxy)-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.5 (br s, 1), 9.4 (s, 1), 8.4 (s, 1), 8.2 (m, 1), 8.1 (d, 1), 7.9 (d, 1), 7.4 (s, 1), 7.3 (s, 1), 4.4 (m, 2), 4.3 (m, 2), 4.0 (m, 1), 3.7 (m, 2), 3.4 (m, 2), 3.3 (s, 3), 3.1 (m, 2), 2.8 (br s, 3) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(2-hydroxyethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-ethoxy-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.4 (s, 1), 8.3 (s, 1), 8.1 (d, 1), 7.9 (d, 1), 7.8 (s, 1), 7.4 (s, 1), 7.3 (s,

1), 7.2 (s, 1), 4.2-4.5 (br, 2), 4.1 (q, 2), 3.7 (m, 2), 3.1 (m, 2), 2.8 (s, 3), 1.3 (t, 3) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-ethyl-*N*'-(2-hydroxyethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2-methoxyethoxy)-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.5 (s, 1), 8.4 (d, 1), 8.2 (s, 1), 8.1 (d, 1), 7.9 (dd, 1), 7.4 (d, 1), 7.3 (d, 1), 4.4 (br d, 2), 4.2 (br t, 2), 3.8 (t, 2), 3.6 (br t, 2), 3.2 (s, 3), 3.2-3.1 (br m, 4), 1.3 (t, 3) ppm.

E. In a manner similar to that described in Paragraph B above, *N*-(5-chloropyridin-2-yl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-hydroxy-5-chlorobenzamide (7.0 g, 13 mmol) reacted with cesium carbonate (29 g, 89 mmol) and 2-bromoethyl methyl ether (2.6 g, 19 mmol) in DMF (100 mL) at 60°C. Purification by flash chromatography on silica gel afforded 4.8 g (62% yield) of *N*-(5-chloropyridin-2-yl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2-methoxyethoxy)-5-chlorobenzamide, as a yellow solid; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.4 (s, 1), 8.4 (s, 1), 8.1 (d, 2), 7.9 (d, 1), 7.4 (s, 1), 7.3 (s, 1), 4.2 (s, 2), 4.2 (br, 2), 3.6 (s, 2), 3.8-3.0 (br, 8), 3.2 (s, 3), 2.9 (s, 3) ppm.

F. In a similar manner, the following compounds were made:

N-(5-chloropyridin-2-yl)-2-[((4-((4-ethylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2-methoxyethoxy)-5-chlorobenzamide; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.5 (s, 1), 8.3 (s, 1), 8.2 (s, 1), 8.1 (d, 1), 7.8 (d, 1), 7.4 (s, 1), 7.2 (s, 1), 8.1 (d, 10, 7.8 (d, 1), 7.4 (s, 1), 7.2 (s, 1), 4.4 (s, 2), 4.3 (s, 2), 3.6 (s, 2), 3.2 (s, 3), 3.8-3.20 (br, 8), 3.2 (q, 2), 1.2 (t, 3) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(methylsulfonyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-((2-(2-methoxyethoxy)ethoxy)-5-chlorobenzamide; (DMSO-d_6/TFA) 9.2 (s, 1), 9.0 (s, 1), 8.3 (d, 1), 8.1 (d, 1), 7.7 (dd,), 7.6 (s, 1), 7.3 (d, 1), 7.1 (d, 1), 4.3 (s, 2), 4.2 (t, 2), 3.9 (t, 2), 3.7 (m, 2), 3.5 (m, 2), 3.4 (s, 3), 2.9 (s, 3), 2.85 (s, 3)ppm; and

N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-3-(ethoxycarbonyl)methoxybenzamide.

G. Other compounds of the invention may be prepared by methods similar to those described in this Example and by methods known to those of ordinary skill in the art.

EXAMPLE 12

Compounds of Formula (Is)

A. To a solution of *N*-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(methylsulfonyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2,3-epoxypropoxy)-5-

chlorobenzamide (0.20 g, 0.30 mmol) in DMF (20 mL) was added imidazole sodium salt (0.15 g, 1.6 mmol) and the mixture stirred at ambient temperature. After 18 hours, the mixture was concentrated of all volatiles *in vacuo*, and the residue dissolved in acetonitrile, water and trifluoroacetic acid. Purification by HPLC on a C18 Dynamax column with 20-80% acetonitrile in water gradient with 0.1% trifluoroacetic acid afforded *N*-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(methylsulfonyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2-hydroxy-3-(imidazol-1-yl)propoxy)-5-chlorobenzamide, trifluoroacetic acid salt as a white solid; NMR (DMSO-d_6/TFA) 11.0 (s, 1), 9.6 (s, 1), 9.0 (s, 1), 8.3 (d, 1), 8.1 (d, 1), 7.9 (dd, 1), 7.8 (s, 1), 7.6 (d, 2), 7.4 (d, 1), 7.3 (d, 1), 4.4-4.3 (m, 2), 4.25 (br m, 1), 4.2 (s, 2), 4.1-4.0 (br m, 2), 2.9 (s, 3), 2.7 (s, 3) ppm.

B. In a similar manner, the following compounds were made:

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-((dimethylamino)sulfonyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2-hydroxy-3-(pyrrolidin-1-yl)propoxy)-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 11.0 (s, 1), 9.6 (s, 1), 8.4 (d, 1), 8.1 (d, 1), 7.9 (dd, 1), 7.8 (s, 1), 7.4 (d, 1), 7.3 (d, 1), 4.3 (s, 2), 4.2 (br m, 1), 4.1 (br s, 2), 3.5 (br m, 2), 3.3 (br m, 2), 3.0 (br m, 2), 2.8 (s, 9), 2.7 (s, 3), 2.0-1.8 (br m, 4) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(methylsulfonyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2-hydroxy-3-(pyrrolidin-1-yl)propoxy)-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 11.0 (s, 1), 9.5 (s, 1), 8.3 (d, 1), 8.1 (d, 1), 7.8 (dd, 1), 7.7 (s, 1), 7.4 (d, 1), 7.3 (d, 1), 4.2 (s, 2), 4.2 (br m, 1), 4.1 (br s, 2), 3.5 (br m, 2), 3.3 (br m, 2), 3.0 (br m, 2), 2.9 (s, 3), 2.7 (s, 3), 2.0-1.8 (br m, 4) ppm.

C. Other compounds of the invention may be prepared by methods similar to those described in this Example and by methods known to those of ordinary skill in the art.

EXAMPLE 13

Compounds of Formula (It)

A. To a solution of *N*-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(methylsulfonyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2,3-epoxypropoxy)-5-chlorobenzamide (0.20 g, 0.30 mmol) in methylene chloride (3 mL) was added methanol (5 mL), followed by 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) (0.040 g, 0.20 mmol) and the mixture stirred at ambient temperature. After 48 hours, the reaction was quenched with aqueous $NaHCO_3$ solution and extracted with methylene chloride. The organic layer was dried over Na_2SO_4 and concentrated *in vacuo*. Purification by flash chromatography on silica gel, followed by precipitation from methylene chloride-hexane afforded 0.080 g (38% yield) of

N-(5-chloropyridin-2-yl)-2-[[(4-((*N*'-methyl-*N*'-(methylsulfonyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2-hydroxy-3-methoxypropoxy)-5-chlorobenzamide, as a pale brown solid: NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.4 (s, 1), 8.3 (d, 1), 8.1 (d, 1), 7.9 (dd, 1), 7.8 (s, 1), 7.4 (s, 1), 7.2 (s, 1), 4.2 (s, 2), 4.1-4.0 (br m, 2), 4.0-3.9 (m, 1), 3.4-3.3 (m, 1), 3.2 (s, 3), 2.9 (s, 3), 2.7 (s, 3) ppm.

B. Other compounds of the invention may be prepared by methods similar to those described in this Example and by methods known to those of ordinary skill in the art.

EXAMPLE 14

Compounds of Formula (Iv)

A. A solution of *N*-(4-chlorophenyl)-2-[(3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-4,5-difluorobenzamide (0.045 g, 0.090 mmol) in 1-methylpiperazine (1 mL, 10.0 mmol) was heated at 85°C for 15 hours. Concentration and purification by HPLC on a C18 Dynamax column with 20-70% acetonitrile in water gradient with 0.1% trifluoroacetic acid afforded *N*-(4-chlorophenyl)-2-[(3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-4-(4-methylpiperazin-1-yl)-5-fluorobenzamide, trifluoroacetic acid salt as a white solid; NMR (DMSO-d_6/TFA) 12.0 (s, 1), 10.4 (s, 1), 9.9 (br s, 1), 8.3 (d, 1), 8.0 (m, 1), 7.9 (m, 1), 7.8 (d, 1), 7.7 (d, 2), 7.6 (m, 2), 7.3 (d, 2), 3.7 (d, 2), 3.6 (d, 2), 3.2 (m, 4), 2.9 (s, 3) ppm.

B. In a similar manner, the following compounds were made:

N-(4-chlorophenyl)-2-[(3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-4-((3-(4-methylpiperazin-1-yl)propyl)amino)-5-fluorobenzamide; NMR (DMSO-d_6/TFA) 12.5 (s, 1), 10.2 (s, 1), 8.1 (m, 1), 8.0 (d, 1), 7.9 (m, 1), 7.8 (d, 1), 7.7 (d, 2), 7.6 (m, 2), 7.4 (d, 2), 3.2-4.0 (m, 12), 2.9 (s, 3), 2.0 (m, 2) ppm;

N-(4-chlorophenyl)-2-[(3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-4-(*N*'-methyl-*N*'-(3-(dimethylamino)propylamino-5-fluorobenzamide;

C. 2-Dimethylaminoethanethiol hydrochloride (1.4 g, 10 mmol) was stirred in aqueous Na_2CO_3 (15% solution, 20 mL) for 0.5 hour. The solution was extracted with ethyl acetate (40 mL) and the organic layer was dried over Na_2SO_4, and concentrated *in vacuo*. To a solution of the residual oil in DMF (1.0 mL) was added *N*-(4-chlorophenyl)-2-[(3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-4,5-difluorobenzamide (0.45 g, 0.09 mmol) and mixture was heated at 105°C. After 15 hours, the mixture was cooled to ambient temperature and concentrated *in vacuo*. Purification by HPLC on a C18 Dynamax column with 20-70% acetonitrile in water gradient with 0.1% trifluoroacetic acid afforded *N*-(4-chlorophenyl)-2-[((3-((2-(dimethylamino)ethyl)thio)benzo[*b*]thien-2-yl)carbonyl)amino]-4-((2-(dimethylamino)ethyl)thio)-5-fluorobenzamide, trifluoroacetic acid salt as tan solid; NMR

(DMSO-d_6/TFA) 11.6 (s, 1), 10.7 (s, 1), 9.8 (br s, 1), 9.4 (br s, 1), 8.4 (d, 1), 8.0 (dd, 2), 7.8 (d, 1), 7.7 (d, 2), 7.5 (m, 2), 7.4 (d, 2), 3.4 (br m, 4), 3.2 (br m, 4), 2.8 (s, 6), 2.6 (s, 6) ppm.

D. Other compounds of the invention may be prepared by methods similar to those described in this Example and by methods known to those of ordinary skill in the art.

EXAMPLE 15

Compounds of Formula (Ip)

A. To a solution of *N*-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(methylsulfonyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, (4.6 g, 8.0 mmol) in methylene chloride (120 mL) was added boron tribromide (1 M solution in methylene chloride, 80 mL, 80 mmol). After 18 hours, the mixture was poured slowly onto ice (ca. 300 g). Ethyl acetate (300 mL) was added, and the aqueous layer was adjusted to pH 7 with saturated aqueous $NaHCO_3$ solution. The layers were separated and the aqueous layer further extracted with ethyl acetate (300 mL). The combined organics were dried over Na_2SO_4 and concentrated *in vacuo* to afford 4.5 g (100% yield) of *N*-(5-chloropyridin-2-yl)-2-[[(4-((*N*'-methyl-*N*'-(methylsulfonyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-hydroxy-5-chlorobenzamide, as a tan solid; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.3 (s, 1), 8.3 (d, 1), 8.1 (d, 1), 7.8 (dd, 1), 7.7 (s, 1), 7.1 (dd, 2), 4.2 (s, 2), 2.9 (s, 3), 2.7 (s, 3) ppm.

B. In a similar manner, the following compounds were made:

N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-3-hydroxy-5-chlorobenzamide; NMR(DMSO-d_6) 10.6 (s, 1), 10.4 (s, 1), 9.6 (s, 1), 8.1 (m, 1), 7.9 (m, 1), 7.7 (d, 2), 7.6 (m, 2), 7.4 (d, 2), 7.1 (d, 2) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(oxazolin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-hydroxy-5-chlorobenzamide; NMR (DMSO-d_6/TFA) 11.0 (br s, 1), 9.4 (br s, 1), 8.3 (s, 1), 8.1 (d, 1), 7.9 (dd, 1), 7.8 (s, 1), 7.4 (s, 2), 7.3 (t, 2), 7.1 (s, 1), 7.0 (s, 1) 4.6 (t, 2), 3.9 (s, 3) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-((dimethylamino)sulfonyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-hydroxy-5-chlorobenzamide; NMR (DMSO-d_6/TFA) 10.8 (s, 1), 9.3 (s, 1), 8.3 (d, 1), 8.1 (d, 1), 7.8 (dd, 1), 7.7 (s, 1), 7.1 (d, 2), 4.2 (s, 2), 2.7 (s, 6), 2.65 (s, 3) ppm;

N-phenyl-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-4,5-dihydroxybenzamide;

N-phenyl-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-3-hydroxybenzamide;

N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-3-hydroxybenzamide; and

N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-4,5-dihydroxybenzamide.

C. Other compounds of the invention may be prepared by methods similar to those described in this Example and by methods known to those of ordinary skill in the art.

EXAMPLE 16

Compounds of Formula (Ib)

A. To a solution of *N*-(4-chlorophenyl)-2-amino-5-methylbenzamide (0.11 g, 0.42 mmol) in pyridine (5 mL) at 0°C was added 2-chlorocarbonyl-3-chlorobenzo[*b*]thiophene (0.15 g, 0.64 mmol), and the mixture allowed to warm to ambient temperature with stirring. After 16 hours, the mixture was poured onto water (5 mL) and the resulting white solid collected by filtration and dried *in vacuo*. Recrystallization from acetonitrile afforded 0.095 g (50% yield) of *N*-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-5-methylbenzamide, as a white crystalline solid; NMR (DMSO-d_6/TFA) 11.4 (s, 1), 10.7 (s, 1), 8.2 (d, 1), 7.4-8.2 (m, 10), 2.4 (s, 3) ppm.

B. In a similar manner, the following compounds were made:

N-(4-bromophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-5-methylbenzamide; NMR (DMSO-d_6/TFA) 11.3 (s, 1), 10.7 (s, 1), 8.2 (d, 1), 7.4-8.2 (m, 10), 2.4 (s, 3) ppm;

N-(4-bromophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-5-chlorobenzamide; NMR (DMSO-d_6/TFA) 11.4 (s, 1), 10.8 (s, 1), 8.4 (d, 1), 7.5-8.2 (m, 10) ppm;

N-(4-chlorophenyl)-2-[((3-chloro-6-methylbenzo[*b*]thien-2-yl)carbonyl)amino]-5-chlorobenzamide; NMR (DMSO-d_6/TFA) 11.3 (s, 1), 10.8 (s, 1), 8.3 (d, 1), 7.4-7.9 (m, 9), 2.5 (s, 3) ppm;

N-(4-chlorophenyl)-2-[((3-methylbenzo[*b*]thien-2-yl)carbonyl)amino]-5-chlorobenzamide; NMR (DMSO-d_6/TFA) 11.2 (s, 1), 10.7 (s, 1), 8.4 (d, 1), 7.4-8.0 (m, 10), 2.8 (s, 3) ppm;

N-(5-chloropyridin-2-yl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-5-methylbenzamide; NMR (DMSO-d_6/TFA) 11.3 (s, 1), 11.2 (s, 1), 8.4 (d, 1), 7.4-8.2 (m, 9), 2.4 (s, 3) ppm;

N-(4-chlorophenyl)-2-[((5-methyl-3-chlorothiophen-2-yl)carbonyl)amino]-5-chlorobenzamide; NMR (DMSO-d_6/TFA) 11.0 (s, 1), 10.8 (s, 1), 8.3 (d, 1), 7.4-7.9 (m, 6), 7.0 (d, 2) 2.5 (d, 3) ppm;

N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-5-fluorobenzamide; NMR (DMSO-d_6/TFA) 11.7 (s, 1), 11.2 (s, 1), 8.3 (dd, 1), 8.2 (m, 1), 7.9 (m, 1), 8.0 (d, 2), 7.7 (d, 1), 7.6 (m, 1), 7.5 (dt, 1), 7.4 (d, 2) ppm;

N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-4-methylbenzamide; NMR (DMSO-d_6/TFA) 11.6 (s, 1), 10.6 (s, 1), 8.2 (s, 1), 8.1 (dd, 1), 7.9 (dd, 1), 7.8 (d, 1), 7.7 (d, 2), 7.6 (s, 1), 7.5 (d, 1), 7.4 (d, 2), 7.1 (d, 1), 2.4 (s, 3) ppm;

N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-3-methyl-5-

chlorobenzamide; NMR (DMSO-d_6/TFA) 10.6 (s, 1), 10.2 (s, 1), 8.1 (dd, 1), 7.9 (dd, 1), 7.7 (d, 2), 7.6-7.5 (m, 4), 7.4 (d, 2), 2.4 (s, 3) ppm;

N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-5-chlorobenzamide; NMR (DMSO-d_6/TFA) 11.4 (s, 1), 10.8 (s, 1), 8.4 (d, 1), 7.4-8.1 (m, 10) ppm;

N-(4-chlorophenyl)-2-[((3-methoxybenzo[*b*]thien-2-yl)carbonyl)amino]-5-methylbenzamide; NMR (DMSO-d_6) 11.4 (s, 1), 10.7 (s, 1), 8.4 (d, 1), 8.0 (m, 2), 7.8 (d, 2), 7.6 (s, 1), 7.4 (m, 5), 4.2 (s, 3), 2.3 (s, 3) ppm;

N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]benzamide; NMR (DMSO-d_6) 11.4 (s, 1), 10.7 (s, 1), 8.4 (d, 2), 8.1 (m, 1), 7.9 (m, 1), 7.9 (d, 1), 7.8 (d, 2), 7.6 (m, 3), 7.4 (d, 2), 7.3 (t, 1) ppm;

N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-4,5-difluorobenzamide; NMR (DMSO-d_6) 11.6 (s, 1), 10.7 (s, 1), 8.4 (dd, 1), 8.1 (m, 2), 8.0 (d, 1), 7.8 (d, 2), 7.6 (m, 2), 7.4 (d, 2) ppm;

N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide; NMR (DMSO-d_6) 10.5 (s, 1), 9.8 (s, 1), 8.1 (m, 1), 7.9 (m, 1), 7.7 (d, 2), 7.6 (m, 2), 7.4 (s, 1), 7.4 (d, 2), 7.3 (s, 1), 3.9 (s, 3) ppm;

N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-4-fluoro-5-chlorobenzamide; NMR (DMSO-d_6) 11.7 (s, 1), 10.8 (s, 1), 8.4 (d, 1), 8.2 (m, 2), 8.0 (d, 1), 7.7 (d, 2), 7.6 (m, 2), 7.4 (d, 2) ppm;

N-(4-chlorophenyl)-2-[((3-methylthiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((4-methyl-3-chlorothiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-phenyl-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-5-methylbenzamide;

N-(pyridin-3-yl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-5-methylbenzamide;

N-(2,4-difluorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-5-methylbenzamide;

N-(pyridin-2-yl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-5-methylbenzamide;

N-(4-methoxyphenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-5-methylbenzamide;

N-(3-fluorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-5-methylbenzamide;

N-(3-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-5-methylbenzamide;

N-(3-methylphenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-5-methylbenzamide;

N-(4-chloro-2-methylphenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-5-methylbenzamide;

N-(4-cyanophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-5-methylbenzamide;

N-(4-fluorophenyl)-2-[((benzo[*b*]thien-2-yl)carbonyl)amino]-5-methylbenzamide;

N-(4-fluorophenyl)-2-[((3-chlorothiophen-2-yl)carbonyl)amino]-5-methylbenzamide;

N-(4-fluorophenyl)-2-[((3-methylbenzo[*b*]thien-2-yl)carbonyl)amino]-5-methylbenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-4-(methylsulfonyl)thiophen-2-yl)carbonyl)amino]-5-methylbenzamide;

N-(4-chlorophenyl)-2-[((3-chlorothiophen-2-yl)carbonyl)amino]-5-methylbenzamide;

N-(4-chlorophenyl)-2-[((3-methoxybenzo[*b*]thien-2-yl)carbonyl)amino]-5-methylbenzamide;

N-(4-chlorophenyl)-2-[((3-bromothiophen-2-yl)carbonyl)amino]-5-methylbenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-4-((1-methylethyl)sulfonyl)thiophen-2-yl)carbonyl)amino]-5-methylbenzamide;

N-(4-chlorophenyl)-2-[((4-bromo-3-methoxythiophen-2-yl)carbonyl)amino]-5-methylbenzamide;

N-(4-chlorophenyl)-2-[((3-methoxythiophen-2-yl)carbonyl)amino]-5-methylbenzamide;

N-(4-fluorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]benzamide;

N-(4-fluorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-5-methoxybenzamide;

N-phenyl-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-3-methylbenzamide;

N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-4-(trifluoro)methylbenzamide;

N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-5-(4-methylpiperazin-1-yl)benzamide;

N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-5-hydroxybenzamide;

N-phenyl-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-4,5-dimethoxybenzamide;

N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-3-chlorobenzamide;

N-phenyl-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-3-methoxybenzamide;

N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-4-fluorobenzamide;

N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-4-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-3-methoxybenzamide;

N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-6-fluorobenzamide;

N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-4,5-dimethoxybenzamide;

N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-4-methyl-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-3-methylbenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-methyl-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide; NMR (DMSO-d_6/TFA) 10.8 (s, 1), 9.3 (s, 1), 8.3 (d, 1), 8.1 (d, 1), 7.8 (dd, 1), 7.5 (d, 1), 7.3 (dd, 2), 3.9 (s, 3), 2.2 (s, 3) ppm;

N-(5-chloropyridin-2-yl)-2-[(((4-cyano-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((5-nitro-3-methylthiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((4-nitro-3-methylthiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-3-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]pyridin-2-amide;

N-phenyl-2-[((1-bromonaphth-2-yl)carbonyl)amino]-5-methylbenzamide; NMR (DMSO-d_6) 10.9 (s, 1), 10.4 (s, 1), 8.26 (d, 1), 8.16 (d, 1), 8.06 (t, 2), 7.76 (m, 1), 7.6-7.7 (m, 5), 7.46 (d, 1), 7.30 (t, 2), 7.07 (t, 1), 2.4 (s, 3);

N-phenyl-2-[((naphth-2-yl)carbonyl)amino]-5-methylbenzamide; NMR (DMSO-d_6) 11.45 (s, 1), 10.6 (s, 1), 8.5 (s, 1), 8.25 (d, 1), 8.05 (d, 2), 8.0 (d, 1), 7.95 (d, 1), 7.75 (m, 3), 7.6 (m, 2), 7.4 (m, 3), 2.4 (s, 3).

N-(4-chlorophenyl)-3-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]pyridin-4-amide; NMR (DMSO-d_6) 11.1 (s, 1), 10.9 (s, 1), 9.4 (s, 1), 8.6 (d,1), 8.2 (d, 1), 8.0 (d, 1), 7.8 (m, 3), 7.6 (m, 2), 7.4 (d, 2) ppm.

C. A suspension of 2-carboxy-3-chloro-4-(4-methylpiperazin-1-yl)methylthiophene HCl salt (2.0 g, 5.8 mmol) in thionyl chloride (50 mL) was heated at reflux. After 90 hours, the mixture was cooled to ambient temperature and concentrated of all volatiles *in vacuo*. To a suspension of the resulting solid in pyridine (20 mL) at 0°C was added *N*-(5-chloropyridin-2-yl)-2-amino-5-chlorobenzamide (1.5 g, 5.2 mmol) in pyridine (5 mL). The mixture was stirred and allowed to warm gradually to ambient temperature. After 16 hours, the mixture was concentrated of all volatiles *in vacuo*. Purification by flash chromatography on silica gel afforded 2.2g (80% yield) of *N*-(5-chloropyridin-2-yl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-5-chlorobenzamide, as a tan foam; NMR (DMSO-d_6/TFA) 11.4 (s, 1), 11.0 (s, 1), 7.6-8.4 (m, 7), 4.4 (s, 2), 3.0-4.0 (br m, 8), 2.9 (s, 3) ppm.

D. In a similar manner, the following compounds were made:

N-(5-bromopyridin-2-yl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-5-chlorobenzamide; NMR (DMSO-d_6/TFA) 11.4 (s, 1), 11.0 (s, 1), 7.6-8.5 (m, 7), 4.4 (s, 2), 3.0-3.8 (br s, 8), 2.9 (s, 3) ppm;

N-(4-chlorophenyl)-2-[((3-chloro-5-methyl-4-((4-methylpiperazin-1-yl)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-4-methyl-5-((4-methylpiperazin-1-yl)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide; and

N-(4-chlorophenyl)-2-[((3-chloro-4-(thiomorpholin-4-yl)methylthiophen-2-yl)carbonyl)amino]-5-chlorobenzamide; NMR (DMSO-d_6) 11.1 (s, 1), 10.8 (s, 1), 8.3 (d, 1), 7.9 (s, 1), 7.8 (s, 1), 7.6 (m, 3), 7.4 (d, 2), 3.5 (s, 2), 2.6 (m, 8) ppm.

E. To a mixture of sodium 3-chloro-4-(morpholin-4-yl)methyl-2-thiophene carboxylate (1.0 g, 3.9 mmol) and *N*-(4-chlorophenyl)-2-amino-5-chlorobenzamide (0.88 g, 3.1 mmol) in pyridine (20 mL) at -10°C was added $POCl_3$ (0.40 mL, 4.3 mmol). After 45

minutes, the mixture was poured onto ice-water and the resulting solid collected by filtration. Crystallization from 1-butanol afforded 0.26 g (13% yield) of *N*-(4-chlorophenyl)-2-[((4-(morpholin-4-yl)methyl-3-chlorothiophen-2-yl)carbonyl)amino]-5-chlorobenzamide, as a tan solid; NMR (DMSO-d_6) 11.1 (s, 1), 10.8 (s, 1), 8.3 (d, 1), 7.9 (s, 1), 7.8 (s, 1), 7.7 (d, 2), 7.6 (d, 2), 7.4 (d, 3), 3.6 (s, 2), 3.3 (br, 4), 2.4 (br, 4) ppm.

F. In a similar manner, the following compounds were made:

N-(4-chlorophenyl)-2-[((4-(methylamino)sulfonyl-3-methylthiophen-2-yl)carbonyl)amino]-5-methylbenzamide; and

N-(4-chlorophenyl)-2-[((4-((4-methylpiperazin-1-yl)sulfonyl)-3-chlorothiophen-2-yl)carbonyl)amino]-5-chlorobenzamide.

G. To a solution of 2-chlorocarbonyl-3-chloro-4-(2-(*N*-methyl-*N*-*tert*-butoxycarbonylamino)ethyl)thiophene (0.095 g, 0.28 mmol) in methylene chloride (10 mL) was added pyridine (0.056 mL, 0.56 mmol) and *N*-(5-chloropyridin-2-yl)-2-amino-3-methoxy-5-chlorobenzamide (0.096 g, 0.31 mmol) and the mixture was stirred at ambient temperature. After 4 days at ambient temperature, the reaction mixture was concentrated *in vacuo* and dissolved in methylene chloride. Trifluoroacetic acid was added and the reaction mixture was stirred for 2 days at ambient temperature. The reaction was quenched with saturated aqueous $NaHCO_3$ solution and extracted with methylene chloride. The combined extracts were dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The product was purified by HPLC on a C18 Dynamax column with 25-95% acetonitrile in water gradient with 0.1% trifluoroacetic acid to afford 0.054 g of *N*-(5-chloropyridin-2-yl)-2-[((4-(2-methylaminoethyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt, as a white solid; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.3 (s, 1), 8.4 (br s, 2), 8.2 (s, 1), 8.1 (d, 1), 7.8 (dd, 1), 7.6 (s, 1), 7.2 (s, 2), 3.8 (s, 3), 3.1 (br s, 2), 2.9 (m, 2), 2.5 (d, 3) ppm.

H. Other compounds of the invention may be prepared by methods similar to those described in this Example and by methods known to those of ordinary skill in the art.

EXAMPLE 17

A. To a solution of *N*-(5-chloropyridin-2-yl)-2-[((4-((methylamino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(morpholin-4-yl)-5-chlorobenzamide (0.20 g, 0.37 mmol) in methylene chloride (5 mL) were added potassium carbonate (0.10 g, 0.74 mmol) and cyanogen bromide (5.0 M in acetonitrile, 0.10 mL, 0.50 mmol) and the mixture stirred at ambient temperature. After 2 hours, water (10 mL) was added and the mixture extracted with ethyl acetate (3x20 mL). The combined organics were washed with brine (10 mL), dried over Na_2SO_4, and concentrated *in vacuo*. Purification by flash chromatography on silica gel

afforded 0.1 g of *N*-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-cyanoamino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(morpholin-4-yl)-5-chlorobenzamide. The resulting product material was dissolved in toluene (10 mL), and sodium azide (0.058 g, 088 mmol) and tributyltin chloride (0.29 g, 0.88 mmol) were added. The mixture was heated at reflux for 2 hours, then cooled to ambient temperature and poured onto brine (10 mL). The mixture was extracted with ethyl acetate (3x20 mL) and the combined organics washed with brine (10 mL), dried over Na_2SO_4, and concentrated *in vacuo*. Purification by HPLC on a C18 Dynamax column with 20-80% acetonitrile in water gradient with 0.1 % trifluoroacetic acid afforded *N*-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(tetrazol-5-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(morpholin-4-yl)-5-chlorobenzamide, trifluoroacetic acid salt as a white solid; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.5 (s, 1), 8.3 (s, 1), 8.1 (m, 1), 7.9 (m, 1), 7.7 (s, 1), 7.4 (m, 2), 4.6 (s, 2), 3.7 (m, 4), 3.0 (s, 3), 2.9 (m, 4) ppm.

B. In a similar manner, the following compounds were made:

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(tetrazol-5-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.3 (s, 1), 8.3 (s, 1), 8.0 (m, 1), 7.8 (m, 1), 7.6 (s, 1), 7.2 (m, 2), 4.5 (s, 2), 3.8 (s, 3), 3.0 (s, 3) ppm.

C. In a manner similar to that described in Paragraph A above, *N*-(5-chloropyridin-2-yl)-2-[((4-((ethylamino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide (0.60 g, 1.2 mmol) reacted with cyanogen bromide (5 M in acetonitrile, 0.6 mL, 3.0 mmol) and potassium carbonate (0.56 g, 4.0 mmol) in CH_2Cl_2 to afford *N*-(5-chloropyridin-2-yl)-2-[((4-((*N*'-ethyl-*N*'-cyanoamino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide. This material reacted with sodium azide (0.25 g, 3.8 mmol) and tributyltin chloride (1.3 g, 3.9 mmol) in toluene. Purification by flash chromatography on silica gel afforded 0.37g (53% yield) of *N*-(5-chloropyridin-2-yl)-2-[((4-((*N*'-ethyl-*N*'-(tetrazol-5-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.4 (s, 1), 8.3 (s, 1), 8.1 (m, 1), 7.9 (m, 1), 7.6 (s, 1), 7.2-7.4 (m, 2), 4.5 (s, 2), 4.0 (m, 2), 3.9 (s, 3), 1.1 (m, 3) ppm.

D. Other compounds of the invention may be prepared by methods similar to those described in this Example and by methods known to those of ordinary skill in the art.

EXAMPLE 18

A. To a solution of *N*-(5-chloropyridin-2-yl)-2-[((4-((*N*'-(2-hydroxyethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(morpholin-4-yl)-5-chlorobenzamide (0.29g, 0.50 mmol) in MeOH were added cyanogen bromide (5 M in

acetonitrile, 0.1 mL, 0.5 mmol) and K_2CO_3 (0.5g, 3.6 mmol) and the reaction was stirred at ambient temperature. After 1 hour, the mixture was poured onto ethyl acetate and H_2O, and the layers separated. The organic layer was dried over $MgSO_4$, and concentrated *in vacuo*. Purification by flash chromatography on silica gel afforded 0.25 g (82% yield) of *N*-(5-chloropyridin-2-yl)-2-[((4-((2-iminotetrahydrooxazol-3-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(morpholin-4-yl)-5-chlorobenzamide, as a yellow solid; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.6 (s, 1), 9.5 (s, 1), 9.2 (s, 1), 7.4-8.4 (m, 6), 4.8 (t, 2), 4.6 (s, 2), 3.7 (t, 2), 3.6 (s, 4), 2.9 (s, 4) ppm.

B. To a solution of *N*-(5-chloropyridin-2-yl)-2-[((4-(chloromethyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide (0.30 g, 0.59 mmol) in DMF (5 mL) was added 2-hydroxy-3-methoxypropylamine (1.0 g, 9.5 mmol) and the mixture was stirred at ambient temperature. After 16 hours, the mixture was acidified with trifluoroacetic acid and purified by HPLC on a C18 Dynamax column with 20-60% acetonitrile in water gradient with 0.1% trifluoroacetic acid. To a solution of the resulting material in methanol (5 mL) were added cyanogen bromide (5 M in acetonitrile, 0.1 mL, 0.5 mmol) and K_2CO_3 (0.3 g, 2.2) and the reaction was stirred at ambient temperature. After 3 hours, the mixture was partitioned between ethyl acetate and water, and the organic layer concentrated *in vacuo*. Purification by HPLC on a C18 Dynamax column with 20-60% acetonitrile in water gradient with 0.1% trifluoroacetic acid afforded *N*-(5-chloropyridin-2-yl)-2-[((4-((2-imino-5-(methoxymethyl)oxazolidin-3-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt as a white solid: NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.6 (s, 1), 9.4 (s, 1), 9.2 (s, 1), 7.2-8.3 (m, 6), 5.2 (s, 1), 4.6 (m, 2), 3.8-4.0 (m, 2), 3.9 (s, 3), 3.5-3.7 (m, 2), 3.3 (s, 3) ppm.

C. In a manner similar to that described in Paragraph A above, to a solution of *N*-(5-chloropyridin-2-yl)-2-[((4-((*N*'-(2-aminoethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide (0.57 g, 1.08 mmol) in methanol (20 mL) were added sodium acetate (0.18 g, 2.16 mmol) and cyanogen bromide (0.26 mL of 5 M solution in acetonitrile, 1.29 mmol). After stirring for 3 hours at ambient temperature, the reaction mixture was concentrated and saturated $NaHCO_3$ (aq) was added. The reaction mixture was extracted with methylene chloride, and the combined extracts were dried over Na_2SO_4. The resulting product was filtered, concentrated, and purified by HPLC on a C18 Dynamax column with 20-95% acetonitrile in water gradient with 0.1% trifluoroacetic acid to afford 0.37 g of *N*-(5-chloropyridin-2-yl)-2-[((4-((2-imino-tetrahydroimidazol-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt, as

a white solid; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.4 (s, 1), 8.3 (s, 1), 8.1 (d, 2), 8.0 (br s, 1), 7.8 (dd, 1), 7.75 (s, 1), 7.3 (d, 2), 4.5 (s, 2), 3.8 (s, 3), 3.5 (s, 4) ppm.

D. In a similar manner, the following compounds were made:

N-(5-chloropyridin-2-yl)-2-[((4-((*trans*-4,5-dimethyl-2-iminotetrahydrooxazol-3-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 9.1 (s, 1), 8.3 (d, 1), 8.0 (d, 1), 7.6 (dd, 1), 7.5 (s, 1), 7.4 (s, 1), 7.3 (s, 1), 7.2 (d, 1), 7.1 (d, 1), 3.9 (m, 5), 3.6 (d, 1), 3.3 (m, 1), 2.5 (m, 1), 1.2 (d, 3), 1.1 (d, 3) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((*cis*-4,5-dimethyl-2-iminotetrahydrooxazol-3-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 9.1 (d, 2), 8.3 (d, 1), 8.0 (d, 1), 7.6 (dd, 1), 7.5 (s, 1), 7.4 (s, 1), 7.3 (s, 1), 7.2 (d, 1), 7.1 (d, 1), 3.9 (m, 6), 3.3 (m, 1), 2.7 (m, 1), 1.2 (d, 3), 1.1 (d, 3) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((2-imino-4-oxoimidazolin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.3 (s., 1), 8.3 (d, 1), 8.1 (m, 2), 7.7 (d, 1), 7.6 (d, 1), 7.5 (s, 1), 7.3 (d, 1), 7.2 (d, 1), 4.4 (s, 2), 4.3 (s, 2), 3.8 (s, 3) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((2-imino-4-(hydroxymethyl)tetrahydrooxazol-3-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.9 (s, 1),), 9.5 (br s, 1), 9.4 (s, 1), 9.2 (br s, 1), 8.3 (s, 1), 8.1 (d, 1), 8.0 (s, 1), 7.8 (dd, 1), 7.3 (d, 2), 4.8 (m, 2), 4.5 (m, 2), 4.1 (m, 2), 3.8 (s, 3), 3.7 (d, 1), 3.4 (d, 2) ppm; and

N-(5-chloropyridin-2-yl)-2-[((4-((tetrahydro-2-imino-2*H*-pyrimidin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.85 (s, 1), 9.30 (s, 1), 8.30 (d, 1), 8.10 (d, 1), 7.80 (m, 2), 7.65 (s, 1), 7.20-7.30 (m, 4), 4.45 (s. 2), 3.80 (s, 3), 3.20-3.30 (m, 4), 1.90 (m, 2) ppm.

E. To a mixture of *N*-(5-chloropyridin-2-yl)-2-[((4-((methylamino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide (1.0 g, 2.0 mmol) and K_2CO_3 (0.97 g, 7.0 mmol) in acetonitrile (20 mL) was added cyanogen bromide (0.8 mL of a 5 M solution in acetonitrile, 4.0 mmol). After stirring at ambient temperature for 3 hours, the reaction was poured into water and extracted with ethyl acetate. The ethyl acetate extract was concentrated *in vacuo* and was purified by flash chromatography on silica gel to give 1.2 g of *N*-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-cyanoamino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.4 (s, 1),

8.3 (d, 1), 8.1 (m, 2), 7.8 (dd, 1), 7.7 (s, 1), 7.4 (d, 1), 7.3 (d, 1), 4.3 (s, 2), 3.9 (s, 3), 2.9 (s, 3) ppm.

F. Other compounds of the invention may be prepared by methods similar to those described in this Example and by methods known to those of ordinary skill in the art.

EXAMPLE 19

A. To a suspension of *N*-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methylureido)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide (0.10 g, 0.20 mmol) in ethanol (5 mL) was added chloroacetaldehyde diethylacetal (0.3 mL, 2.0 mmol). The mixture was heated at reflux for 4 days, then cooled to ambient temperature and poured onto water. The mixture was neutralized by addition of saturated $NaHCO_3$ solution and the solid collected by filtration. Purification by HPLC on a C18 Dynamax column with 20-80% acetonitrile in water gradient with 0.1% trifluoroacetic acid afforded *N*-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-(oxazol-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt as a white solid: NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.4 (s, 1), 8.4 (d, 1), 8.1 (d, 1), 7.9 (dd, 1), 7.8 (s, 1), 7.6 (s, 1), 7.4 (d, 1), 7.3 (d, 1), 7.0 (s, 1), 4.5 (s, 2), 3.8 (s, 3), 3.0 (s, 3) ppm.

B. Other compounds of the invention may be prepared by methods similar to those described in this Example and by methods known to those of ordinary skill in the art.

EXAMPLE 20

A. To a solution of *N*-(4-chlorophenyl)-2-[((3-chloro-4-((((2-hydroxyethoxy)ethyl)amino)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide (0.25 g, 0.46 mmol) in acetonitrile (5 mL) was added formaldehyde (0.19 mL of a 37% solution in water, 2.3 mmol), followed by $NaCNBH_3$ (0.045 g, 0.69 mmol) and the mixture stirred at ambient temperature. After 2 hours, the mixture was concentrated of all volatiles *in vacuo*. Purification by HPLC on a C18 Dynamax column with acetonitrile in water gradient with 0.1% trifluoroacetic acid afforded *N*-(4-chlorophenyl)-2-[((3-chloro-4-((*N'*-methyl-*N'*-(2-(hydroxyethoxy)ethyl)amino)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide, trifluoroacetic acid salt as a white solid; NMR (DMSO-d_6/TFA) 11.2 (s, 1), 10.8 (s, 1), 9.6 (br s, 1), 8.4 (d, 1), 8.3 (s, 1), 7.9 (s, 1), 7.7 (d, 2), 7.6 (d, 1), 7.4 (d, 2), 4.5 (d, 1), 4.3 (d, 1), 3.8 (m, 2), 3.5 (m, 4), 3.4 (br s, 1), 2.8 (s, 3) ppm.

B. In a similar manner, the following compounds were made:

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-(2-(hydroxyethoxy)ethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid

salt; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.6 (br s, 1), 9.5 (s, 1), 8.4 (s, 1), 8.2 (s, 1), 8.1 (d, 1), 7.9 (d, 1), 7.4 (s, 1), 7.3 (s, 1), 4.5 (d, 1), 4.3 (d, 1), 3.9 (s, 3), 3.8 (m, 2), 3.5 (m, 4), 3.4 (br s, 2), 2.8 (s, 3) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(4-hydroxycyclohexyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide; NMR ($CDCl_3$) 9.1 (s, 1), 9.0 (s, 1), 7.0-8.2 (m, 6), 4.4 (s, 2), 3.9 (s, 3), 3.6 (m, 1), 3.5 (s, 2), 2.5 (m, 1), 2.2 (s, 3), 1.8-2.1 (m, 4), 1.4 (m, 4) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-ethyl-*N*'-((imidazol-2-yl)methyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6) 10.90 (s, 1H), 9.30 (s, 1H), 8.35 (d, 1H), 8.10 (d, 1H), 7.90 (dd, 1H), 7.85 (s, 2H), 7.60 (s, 2H), 7.40 (d, 1H), 7.25 (d, 1H), 4.05 (s, 2H), 3.90 (s, 3H), 3.60 (s, 2H), 2.50 (q, 2H), 1.00 (t, 3H) ppm; and

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-ethyl-*N*'-(4-(dimethylamino)but-3-yn-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6) 10.90-10.85 (m, 1H), 9.40-9.30 (m, 1H0, 8.38 (d, 1H), 8.10 (d, 1H), 7.90 (dd, 1H), 7.65 (s, 1H), 7.60 (s, 1H), 7.39 (d, 1H), 7.25 (d, 1H), 4.42-3.38 (m, 2H), 3.90 (s, 3H), 3.40-3.25 (m, 2H), 2.50 (s, 3H), 2.10-2.00 (m, 3H), 1.10-0.90 (m, 3H) ppm.

C. *N*-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*''-ethylureido)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(4-(*tert*-butoxycarbonyl)piperazin-1-yl)-5-chlorobenzamide, trifluoroacetic acid salt, (~2 g, 2.7 mmol) was dissolved in acetonitrile (40 mL), and acetaldehyde (~1 mL, 18 mmol) was added, followed by a few drops of acetic acid. After one hour, a few more drops of acetic acid were added. After several hours, more acetaldehyde and acetic acid were added and the reaction mixture allowed to stir for 16 hours at ambient temperature. More acetic acid (10 mL) was added and the reaction mixture stirred for one hour, then sodium cyanoborohydride (0.51 g, 8.0 mmol) was added to the reaction mixture. The reaction mixture was stirred for one hour, concentrated *in vacuo*, and the residue taken up in ethyl acetate (100 mL). The ethyl acetate layer was washed with 1 M sodium bicarbonate (2x50mL), brine (50 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The crude product was purified by reverse phase preparatory HPLC and lyophilized to give 0.69 g (28% yield) of the trifluoroacetic acid salt (monohydrate) of the compound, *N*-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*''-ethylureido)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(4-ethylpiperazin-1-yl)-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.4 (s, 1), 8.4 (d, 1), 8.1 (d, 1), 7.9 (dd, 1), 7.5 (s, 1), 7.4 (d, 2),

6.4 (br, 1), 4.3 (s, 2), 3.6 (d, 2), 3.4 (d, 2), 3.2 (d, 3), 3.0 (d, 5), 2.8 (s, 3), 1.2 (t, 3), 1.0 (t, 3) ppm.

D. Other compounds of the invention may be prepared by methods similar to those described in this Example and by methods known to those of ordinary skill in the art.

EXAMPLE 21

A. To a solution of *N*-(4-chlorophenyl)-2-[((3-chloro-5-((4-(ethoxycarbonylmethyl)piperazin-1-yl)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide (0.61 g, 1.0 mmol) in 3:1:1 (volume ratio) tetrahydrofuran/methanol/water (35 mL) was added lithium hydroxide monohydrate (0.12 g, 3.0 mmol). The solution was stirred at ambient temperature for 1 hour, then diluted with water (25 mL), adjusted to pH 3 by addition of 1 N HCl and concentrated *in vacuo* to remove the tetrahydrofuran and methanol. The residual oil was diluted with acetonitrile, water and trifluoroacetic acid and purified by HPLC on a C18 Dynamax column with 50-65% acetonitrile in water gradient with 0.1% trifluoroacetic acid to afford *N*-(4-chlorophenyl)-2-[((3-chloro-5-((4-(carboxymethyl)piperazin-1-yl)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide, trifluoroacetic acid salt as a white solid: NMR (DMSO-d_6/TFA) 11.2 (s, 1), 10.8 (s, 1), 8.3 (d, 1), 7.9 (d, 1), 7.3-7.7 (m, 6), 4.4 (s, 2) 4.2 (s, 2), 3.4 (br s, 4), 3.2 (br s, 4) ppm.

B. In a similar manner, the following compounds were made:

N-(4-chlorophenyl)-2-[((3-chloro-6-(4-(carboxymethyl)piperazin-1-yl)methylbenzo[*b*]thien-2-yl)carbonyl)amino]-5-chlorobenzamide; (DMSO-d_6/TFA) 11.4 (s, 1), 10.8 (s, 1), 8.4 (d, 1), 8.3 (br s, 1), 8.1 (d, 1), 8.0 (d, 1), 7.4-7.7 (m, 6), 4.6 (s, 2), 4.2 (s, 2), 3.5 (br s, 8) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(2-hydroxyethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(4-(carboxy)piperidin-1-yl)-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.6 (s, 1), 7.3-8.5 (m, 6), 4.2-4.5 (m, 2), 3.7 (t, 2), 3.6 (s, 3), 3.0-3.3 (m, 4), 2.6-2.9 (m, 4), 1.6-2.0 (m, 4) ppm;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(4-trifluoromethyl-5-carboxypyrimidin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(morpholin-4-yl)-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.5 (s, 1), 8.9 (m, 1), 8.3 (br s, 1), 8.1 (m, 1), 7.8 (m, 1), 7.6 (m, 1), 7.6 (m, 1), 7.4 (s, 2), 4.8 (s, 2), 3.6 (m, 4), 3.2 (s, 3), 2.9 (m, 4) ppm;

N-(4-chlorophenyl)-2-[((3-chloro-5-carboxythiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-5-(*N*'-methyl-*N*'-(carboxymethyl)amino)methylthiophen-2-yl)carbonyl)amino]-5-chlorobenzamide; and

N-(4-chlorophenyl)-2-[((3-chloro-5-(((carboxymethyl)thio)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide.

C. Other compounds of the invention may be prepared by methods similar to those described in this Example and by methods known to those of ordinary skill in the art.

EXAMPLE 22

A. To a suspension of *N*-(4-chlorophenyl)-2-[((3-chloro-5-(thiomorpholin-4-yl)methylthiophen-2-yl)carbonyl)amino]-5-chlorobenzamide (0.1 g, 0.2 mmol) in methanol (20 mL) at 0°C was added a solution of potassium peroxymonosulfate (0.13 g, 0.2 mmol) in water (5 mL). After 5 minutes, the reaction was quenched by addition of aqueous 5% sodium bisulfite solution. The mixture was extracted with methylene chloride/methanol, and the organic phase dried over Na_2SO_4 and concentrated *in vacuo*. Purification by flash chromatography on silica gel afforded 0.064 g (62% yield) of *N*-(4-chlorophenyl)-2-[((3-chloro-5-(1-(oxo)thiomorpholin-4-yl)methylthiophen-2-yl)carbonyl)amino]-5-chlorobenzamide, as a pale yellow powder; NMR (DMSO-d_6/TFA) 11.2 (s, 1), 10.7 (s, 1), 8.3 (d, 1), 7.9 (s, 1), 7.7 (m, 2), 7.6 (m, 1), 7.4 (m, 3), 4.7 (s, 2), 3.7 (m, 2), 3.5 (m. 2), 2.9 (br s, 4) ppm.

B. In a similar manner, the following compounds were made:

N-(4-chlorophenyl)-2-[((3-chloro-5-((methylsulfinyl)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide; NMR (DMSO-d_6) 11.1 (s, 1), 10.8 (s, 1), 8.3 (dd, 1), 7.9 (d, 1), 7.8 (dd, 2), 7.7 (dd, 1), 7.4 (d, 2), 7.2 (s, 1), 4.4 (dd, 2), 3.3 (s, 3) ppm;

N-(4-chlorophenyl)-2-[((3-chloro-5-((methylsulfonyl)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide; NMR (DMSO-d_6) 11.1 (s, 1), 10.8 (s, 1), 8.3 (br d, 1), 7.9 (s, 1), 7.8-7.6 (br m, 3), 7.4 (br d, 2), 7.2 (s, 1), 4.8 (s, 2), 3.0 (s, 3) ppm;

N-(4-chlorophenyl)-2-[((3-chloro-5-(((2-(dimethylamino)ethyl)sulfinyl)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide; NMR (DMSO-d_6) 11:1 (s, 1), 10.8 (s, 1), 8.3 (d, 1), 7.9 (s, 1), 7.7 (d, 2), 7.5 (d, 1), 7.3 (d, 2), 7.2 (s, 1), 4.4 (dd, 2), 3.4 (m, 2), 3.2-2.8 (m, 2), 2.7 (s, 6) ppm;

N-(4-chlorophenyl)-2-[((3-chloro-4-((methylsulfonyl)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide; NMR (DMSO-d_6) 11.1 (s, 1), 10.8 (s, 1), 8.3 (d, 1), 8.1 (s, 1), 7.9 (s, 1), 7.7 (d, 2), 7.6 (dd, 1), 7.4 (d, 2), 4.6 (s, 2), 3.0 (s, 3) ppm;

N-(4-chlorophenyl)-2-[((3-chloro-4-((methylsulfinyl)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide; NMR (DMSO-d_6) 11.1 (s, 1), 10.7 (s, 1), 8.3 (d, 1), 7.9 (s, 1), 7.8 (s, 1), 7.7 (d, 2), 7.6 (dd, 1), 7.4 (d, 2), 4.1 (dd, 2), 2.5 (s, 3) ppm; and

N-(4-chlorophenyl)-2-[((3-chloro-5-(1,1,4-tri(oxo)thiomorpholin-4-yl)methylthiophen-2-yl)carbonyl)amino]-5-chlorobenzamide.

C. To a solution of *N*-(5-chloropyridin-2-yl)-2-[((4-(chloromethyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide (2.0 g, 4.0 mmol) in DMF (40 mL) was added sodium thiomethoxide (1.4 g, 20 mmol). The mixture was stirred at ambient temperature for 16 hours, then poured onto ice water (200 mL), filtered, and dried to give 1.55 g crude product, *N*-(5-chloropyridin-2-yl)-2-[((4-((methylthio)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide. To a solution of the product in CH_2Cl_2 (30 mL) at -20°C was added 3-chloroperoxybenozic acid (mCPBA) (0.71 g, 3.3 mmol) in two equal portions. After 2 hours, the reaction was poured onto ice water (200 mL). The resulting solid was collected by filtration and washed with CH_2Cl_2 (30 mL) and THF (5 mL) to afford 0.72 g (34% yield) of *N*-(5-chloropyridin-2-yl)-2-[((4-((methylsulfinyl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, as a tan solid; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.4 (s, 1), 8.3 (s, 1), 8.1 (d, 1), 7.9 (d, 1), 7.8 (s, 1), 7.4 (s, 1), 7.3 (s, 1), 4.2 (d, 1), 4.0 (d, 1), 3.9 (s, 3), 2.6 (s, 3) ppm.

D. In a similar manner, the following compound was made:
N-(4-chlorophenyl)-2-[((3-chloro-5-(((methoxycarbonylmethyl)sulfinyl)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide.

E. In a manner similar to that described in Paragraph C above, *N*-(5-chloropyridin-2-yl)-2-[((4-(chloromethyl)-3-chlorothiophen-2-yl)carbonyl)amino]--3-methoxy-5-chlorobenzamide (0.20 g, 0.42 mmol) reacted with morpholine (0.18 mL, 2.1 mmol), followed by mCPBA (0.24 g, 0.84 mmol) to afford *N*-(4-chlorophenyl)-2-[((3-chloro-4-((4-oxomorpholin-4-yl)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide. Purification by HPLC on a C18 Dynamax column with 20-80% acetonitrile in water gradient with 0.1% trifluoroacetic acid afforded the trifluoroacetic acid salt as a white solid; NMR (DMSO-d_6/TFA) 11.2 (s, 1), 10.8 (s, 1), 8.4 (d, 1), 8.3 (s, 1), 7.9 (s, 1), 7.7 (d, 2), 7.6 (d, 1), 7.4 (d, 2), 4.9 (s, 2), 3.9 (m, 6), 3.5 (m, 2) ppm.

F. In a similar manner, the following compound was made:
N-(5-chloropyridin-2-yl)-2-[((4-(((2-hydroxyethyl)sulfinyl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide; NMR (DMSO-d_6/TFA) 10.8 (s, 1), 9.4 (s, 1), 8.3 (d, 1), 8.1 (d, 1), 7.8 (m, 1), 7.3 (s, 1), 7.2 (s, 1), 4.2 (d, 1), 4.0 (d, 1), 3.9 (s, 3), 3.8 (m, 2), 2.9 (m, 1), 2.8 (m, 1) ppm.

G. Other compounds of the invention may be prepared by methods similar to those described in this Example and by methods known to those of ordinary skill in the art.

EXAMPLE 23

A. A solution of *N*-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N"*-ethylureido)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(4-(*tert*-butoxycarbonyl)piperazin-1-yl)-5-chlorobenzamide (4.7 g, 6.5 mmol) in methylene chloride (30 mL) and trifluoroacetic acid (3 mL) was stirred at ambient temperature. After one hour, additional trifluoroacetic acid (10 mL) was added and the reaction stirred for an additional 3 hours. The mixture was then concentrated and dried *in vacuo* to *N*-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N"*-ethylureido)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(piperazin-1-yl)-5-chlorobenzamide, trifluoroacetic acid salt as a light brown oil; NMR (DMSO-d_6): 10.9 (s, 1), 9.4 (s, 1), 8.3 (d, 1), 8.1 (d, 1), 7.9 (dd, 1), 7.5 (s, 1), 7.4 (s, 2), 4.3 (s, 2), 3.1 (m, 10), 2.8 (s, 3), 1.0 (t, 3) ppm.

B. Other compounds of the invention may be prepared by methods similar to those described in this Example and by methods known to those of ordinary skill in the art.

EXAMPLE 24

A. *N*-(4-chlorophenyl)-2-[((3-chloro-4-(((2,2-dimethyldioxolan-4-yl)methoxy)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide **9955** (0.10 g, 0.17 mmol) was stirred in a mixture of 1 M HCl (1.0 mL) and THF (1.0 mL) at ambient temperature. After 16 hours, the mixture was poured onto water and extracted with ethyl acetate. The organic layer was dried over Na_2SO_4 and concentrated *in vacuo*. Purification by HPLC on a C18 Dynamax column with acetonitrile in water gradient with 0.1% trifluoroacetic acid afforded *N*-(4-chlorophenyl)-2-[((3-(2,3-dihydroxypropoxy)methylthiophen-2-yl)carbonyl)amino]-5-chlorobenzamide; NMR (DMSO-d_6) 11.0 (s, 1), 10.7 (s, 1), 8.3 (d, 1), 7.9 (d, 2), 7.7 (d, 2), 7.6 (d, 1), 7.4 (d, 2), 4.4 (s, 2), 3.5 (m, 1), 3.4 (m, 1), 3.3 (m, 2) ppm.

B. Other compounds of the invention may be prepared by methods similar to those described in this Example and by methods known to those of ordinary skill in the art.

EXAMPLE 25

A. A solution of *N*-(5-chloropyridin-2-yl)-2-[((4-cyano-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide (0.10 g, 0.21 mmol) in absolute ethanol (15 mL) was cooled to -78°C and HCl(g) was bubbled through the mixture for 15 minutes. The resultant mixture was stirred at ambient temperature in a sealed vessel for 20 hours, then concentrated of all volatiles *in vacuo* without heating. The residue was dissolved in absolute ethanol (10 mL) and treated with 1,2-diaminoethane (0.14 mL, 2.1 mmol) at 60°C. After 1 hour

the mixture was cooled to ambient temperature and concentrated *in vacuo*. Purification by chromatography on silica gel, followed by lyophilization from aqueous trifluoroacetic acid afforded *N*-(5-chloropyridin-2-yl)-2-[((4-(imidazolin-2-yl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt as a yellow solid; NMR ($CDCl_3$) 10.9 (s, 1), 10.4 (s, 1), 9.7 (s, 1), 8.6 (s, 1), 8.3 (d, 1), 8.1 (d, 1), 7.9 (d, 1), 7.3 (d, 2), 4.0 (s, 4), 3.9 (s, 3) ppm.

B. Other compounds of the invention may be prepared by methods similar to those described in this Example and by methods known to those of ordinary skill in the art.

EXAMPLE 26

A. To a solution of *N*-(5-chloropyridin-2-yl)-2-[((4-(chloromethyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide (0.093 g, 0.19 mmol) in methylene chloride (4.0 mL) was added mCPBA (0.044 g, 0.20 mmol) The reaction mixture was stirred at ambient temperature for 16 hours. The mixture was poured into ethyl acetate (20 mL) and washed with saturated aqueous sodium bicarbonate (2x5 mL). The organic layer was dried and concentrated *in vacuo* to give the crude pyridine *N*-oxide. The crude material was dissolved in DMF (3.0 mL) and trimethylethylene diamine (0.115 mL, 0.9 mmol) was added. The reaction was stirred for 16 hours at ambient temperature and poured into water and ethyl acetate. The ethyl acetate layer was washed with water (2x2 mL) and concentrated. Purification by HPLC on a C18 Dynamax column with acetonitrile in water gradient with 0.1% trifluoroacetica acid afforded 0.028 g of *N*-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-(2-(dimethylamino)ethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide *N*-oxide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.6 (br s, 1), 9.8 (s, 1), 8.6 (d, 1), 8.3 (d, 1), 8.2 (s, 1), 7.6 (dd, 1), 7.4 (dd, 2), 4.4 (s, 2), 3.9 (s, 3), 3.6 (s, 4), 2.9 (s, 6), 2.8 (s, 3) ppm.

B. Other compounds of the invention may be prepared by methods similar to those described in this Example and by methods known to those of ordinary skill in the art.

EXAMPLE 27

A. Hydroxylamine hydrochloride (0.58 g, 8.3 mmol) was dissolved in a solution of sodium methoxide prepared by dissolving sodium (0.17 g) in methanol (50 mL). *N*-(5-chloropyridin-2-yl)-2-[((4-cyanomethyl-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide (2.56 g, 5.2 mmol) and additional methanol (30 mL) were then added. The reaction mixture was refluxed for 16 hours, then a solution of hydroxylamine hydrochloride (0.67 g, 9.6 mmol) in sodium methoxide (0.20 g sodium, 25 mL methanol) was added. The

reaction mixture was refluxed for 24 hours, then a solution of hydroxylamine hydrochloride (0.63 g, 9.1 mmol) in sodium methoxide (0.19 g sodium, 60 mL methanol) was added. The reaction mixture was refluxed for an additional 24 hours, filtered hot, concentrated *in vacuo*, and dried under vacuum. Purification by HPLC on a C18 Dynamax column with 20-70% acetonitrile in water gradient with 0.1% trifluoroacetic acid gave *N*-(5-chloropyridin-2-yl)-2-[((4-(2-amino-2-(hydroxyimino)ethyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt, as a white solid; NMR (DMSO-d_6) 10.9 (s, 1), 9.4 (d, 1), 8.9 (br, 1), 8.4 (d, 1), 8.1 (d, 1), 7.9 (dd, 1), 7.8 (s, 0.5), 7.7 (s, 0.5), 7.4 (d, 1), 7.2 (d, 1), 3.9 (s, 3), 3.7 (s, 2) ppm.

B. In a similar manner, the following compound was made:

N-(5-chloropyridin-2-yl)-2-[((4-(*N'*-methyl-*N''*-hydroxyguanidino)methyl-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 10.6 (s, 1), 9.4 (s., 1), 8.4 (d, 1), 8.1 (m, 2), 7.9 (dd, 1), 7.7 (s, 1), 7.4 (d, 1), 7.3 (d, 1), 4.5 (s, 2), 3.9 (s, 3), 3.0 (s, 3) ppm.

C. Other compounds of the invention may be prepared by methods similar to those described in this Example and by methods known to those of ordinary skill in the art.

EXAMPLE 28

A. To *N*-(5-chloropyridin-2-yl)-2-[((4-(chloromethyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide (1.5 g, 3.0 mmol) in DMF (15 mL), was added ethylene diamine (0.09 g, 15 mmol) at ambient temperature. After 2 hours, the reaction was poured into water and extracted with ethyl acetate. The ethyl acetate solution was dried ($NaSO_4$) and concentrated *in vacuo* to afford the crude amine adduct. To the adduct was added triethyl orthoformate (1.33 g, 9 mmol) in acetic acid (20 mL). After stirring at ambient temperature for 1 hour, the reaction was poured into water and extracted with ethyl acetate. The ethyl acetate layer was dried ($NaSO_4$), concentrated *in vacuo*, and purified by HPLC on a C18 Dynamax column with acetonitrile in water gradient with 0.1% trifluoroacetic acid to afford 0.87 g of *N*-(5-chloropyridin-2-yl)-2-[((4-((imidazolin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide (870 mg), trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 10.3 (s., 1), 9.4 (s, 1), 8.6 (d, 2), 8.3 (d, 1), 8.1 (d, 1), 7.8 (dd, 1), 7.3 (d, 1), 7.2 (d, 1), 4.6 (s, 2), 3.7~3.9 (m, 7) ppm.

B. In a similar manner, the following compound was made:

N-(5-chloropyridin-2-yl)-2-[((4-((5-hydroxy-1,4,5,6-tetrahydropyrimidin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.9 (s., 1), 9.4 (s, 1), 8.5 (d, 1), 8.4 (d, 1), 8.1 (d,

1), 8.0 (s, 1), 7.8 (dd, 1), 7.3 (d, 1), 7.2 (d, 1), 4.6 (m, 2), 4.62 (br s, 1), 3.9 (s, 3), 3.1~3.6 (m, 4) ppm.

C. Other compounds of the invention may be prepared by methods similar to those described in this Example and by methods known to those of ordinary skill in the art.

EXAMPLE 29

A. To a mixture of *N*-(5-chloropyridin-2-yl)-2-[((4-((2-aminoimidazol-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide (0.053 g, 0.96 mmol) and sulfuric acid (0.10 g, 1.06 mmol) in methanol (10 mL) was added *N*-chlorosuccinimide (0.192 g, 1.43 mmol). After stirring at ambient temperature for 6 hours, the reaction was poured into water and extracted with ethyl acetate. The ethyl acetate extract was dried over sodium sulfate, concentrated *in vacuo*, and purified by flash chromatography on silica gel to give 0.33 g of *N*-(5-chloropyridin-2-yl)-2-[((4-((*cis*-4,5-dimethoxy-2-iminotetrahydroimidazol-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide; NMR ($CDCl_3$) 9.0 (d, 2), 8.3 (d, 1), 8.1 (d, 1), 7.7 (dd, 1), 7.5 (s, 1), 7.3 (d, 1), 7.1 (d, 1), 6.0 (br s, 1), 4.8 (m, 2), 4.6 (d, 1), 4.3 (d, 1), 3.9 (s, 3), 3.4 (s, 3), 3.3 (s, 3) ppm.

B. Other compounds of the invention may be prepared by methods similar to those described in this Example and by methods known to those of ordinary skill in the art.

EXAMPLE 30

A. To a solution of *N*-(5-chloropyridin-2-yl)-2-[((4-((*N*'-(2-aminoethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide (0.64 g, 1.2 mmol) and triethylamine (0.31 g, 3.1 mmol) in dichloromethane (20 mL) at 0°C was added $POCl_3$ (0.14 g, 0.923 mmol). The reaction was allowed to warm to ambient temperature and stirred for 16 hours. The reaction was quenched with methanol, concentrated *in vacuo*, and purified by HPLC on a C18 Dynamax column with acetonitrile in water gradient with 0.1% trifluoroacetic acid to afford 0.13 g of *N*-(5-chloropyridin-2-yl)-2-[((4-(((2-dimethylphosphoramidoethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.4 (s, 1), 8.9 (br s, 1), 8.4 (d, 1), 8.2 (d, 1), 8.1 (s, 1), 7.9 (dd, 1), 7.4 (s, 1), 7.3 (s, 1), 4.2 (s, 2), 3.9 (s, 3), 3.6 (s, 3), 3.55 (s, 3), 3.1 (m, 4) ppm.

B. Other compounds of the invention may be prepared by methods similar to those described in this Example and by methods known to those of ordinary skill in the art.

EXAMPLE 31

A. To a mixture of *N*-(5-chloropyridin-2-yl)-2-[[(4-((methylamino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide (0.70 g, 1.4 mmol) and triethylamine (0.16 g, 1.5 mmol) in dichloromethane (7 mL) was added ethylene chlorophosphate (0.19 g, 1.5 mmol) at 0°C. The reaction was allowed to warm to ambient temperature and stirred for 2 hours. The reaction was then quenched with methanol. The reaction mixture was poured into water and extracted with ethyl acetate. The ethyl acetate extract was concentrated *in vacuo* and purified by flash chromatography on silica gel to give 0.70 g of *N*-(5-chloropyridin-2-yl)-2-[[(4-((*N'*-methyl-*N'*-(1,3,2-dioxaphospholan-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.4 (d, 1), 8.3 (d, 1), 8.1 (d, 1), 7.9 (dd, 1), 7.7 (s, 1), 7.4 (d, 1), 7.3 (d, 1), 4.4 (m, 4), 4.2 (d, 2), 3.9 (s, 3), 2.6 (d, 3) ppm.

B. Other compounds of the invention may be prepared by methods similar to those described in this Example and by methods known to those of ordinary skill in the art.

EXAMPLE 32

A. A mixture of *N*-(5-chloropyridin-2-yl)-2-[((4-((*N'*-(2-aminoethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide (1.5 g, 2.9 mmol) and triethyl orthochloroacetate (1.3 g, 8.6 mmol) in acetic acid (10 mL) was stirred at ambient temperature for 16 hours. The solvent was removed *in vacuo* and the resulting residue was purified by HPLC on a C18 Dynamax column with acetonitrile in water gradient with 0.1% trifluoroacetic acid to afford 0.14 g of *N*-(5-chloropyridin-2-yl)-2-[((4-((2-(chloromethyl)imidazolin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt. The product (0.14 g, 0.24 mmol) was treated with tetrabutylammonium cyanide (0.097 g, 0.36 mmol) in acetonitrile (3 mL) and the mixture stirred at ambient temperature for 16 hours. It was then purified directly by HPLC on a C18 Dynamax column with acetonitrile in water gradient with 0.1% trifluoroacetic acid to afford 0.020 g of *N*-(5-chloropyridin-2-yl)-2-[((4-((2-(cyanomethyl)imidazolin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.8 (br s, 1), 9.4 (d, 1), 8.4 (d, 1), 8.2 (d, 1), 8.1 (s, 1), 7.9 (dd, 1), 7.4 (d, 1), 7.3 (d, 1), 4.7 (s, 2), 4.5 (br s, 2), 3.7~3.9 (m, 7) ppm.

B. Other compounds of the invention may be prepared by methods similar to those described in this Example and by methods known to those of ordinary skill in the art.

EXAMPLE 33

A. A mixture of *N*-(5-chloropyridin-2-yl)-2-[((4-((2-(methylthio)imidazolin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide (0.60 g, 1.03 mmol) and 2-aminoethanol (0.18 g, 3.1 mmol) was refluxed in isopropanol for 16 hours. After removal of the solvent *in vacuo*, the resulting crude product was purified by HPLC on a C18 Dynamax column with acetonitrile in water gradient with 0.1% trifluoroacetic acid to afford 0.13 g of *N*-(5-chloropyridin-2-yl)-2-[((4-((2-(hydroxyethyl)imino)tetrahydroimidazol-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.4 (d, 1), 8.4 (br s, 2), 8.3 (d, 1), 8.1 (d, 1), 7.7 (m, 1), 7.6 (s, 1), 7.3 (d, 1), 7.2 (d, 1), 4.5 (s, 2), 3.9 (s, 3), 3.4 ~3. 7 (m, 6), 3.2-3.35 (m, 2) ppm.

B. A mixture of *N*-(5-chloropyridin-2-yl)-2-[((4-((2-(methylthio)imidazolin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide (0.88 g, 1.5 mmol), glycinamide hydrochloride (0.33 g, 3.0 mmol) and diisopropylethylamine (0.49 g, 3.8 mmol) in DMF was stirred at 75-80°C for 10 hours. The reaction was then poured into water and extracted with ethyl acetate. The ethyl acetate layer was dried over sodium sulfate, concentrated *in vacuo*, and purified by HPLC on a C18 Dynamax column with acetonitrile in water gradient with 0.1% trifluoroacetic acid to afford 0.47 g of *N*-(5-chloropyridin-2-yl)-2-[((4-((2-(((aminocarbonyl)methyl)imino)tetrahydroimidazol-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 9.4 (d, 1), 8.6 (br s, 2), 8.2 (d, 1), 8.1 (d, 1), 7.6 (m, 2), 7.4 (br s, 1), 7.2 (br s, 1), 4.5 (s, 2), 3.9 (s, 5), 3.6 (m, 4) ppm.

C. Other compounds of the invention may be prepared by methods similar to those described in this Example and by methods known to those of ordinary skill in the art.

EXAMPLE 34

A. A mixture of *N*-(5-chloropyridin-2-yl)-2-[((4-(chloromethyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide (1.0 g, 2.0 mmol) and 2-formylimidazole (1.2 g, 12.5 mmol) in DMF was stirred at 110°C for 10 hours. After cooling to ambient temperature, the reaction mixture was poured into water and extracted with ethyl acetate. The ethyl acetate extract was concentrated *in vacuio* and purified by flash chromatography on silica gel to give the imidazole adduct. To the imidazole adduct in methanol (10 mL) at 0°C was added $NaBH_4$ until thin layer chromatography indicated the completion of the reaction. The reaction was poured into water and extracted with ethyl acetate. The ethyl acetate extract concentrated *in vacuo* and purified by HPLC on a C18 Dynamax column with acetonitrile in water gradient with

0.1% trifluoroacetic acid to afford to give 0.21 g of *N*-(5-chloropyridin-2-yl)-2-[((4-((2-(hydroxymethyl)imidazol-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.4 (d, 1), 8.3 (d, 1), 8.1 (d, 1), 7.9 (m, 2), 7.6 (s, 2), 7.35 (d, 1), 7.25 (d, 1), 5.4 (s, 2), 4.8 (s, 2), 3.9 (s, 3) ppm.

B. Other compounds of the invention may be prepared by methods similar to those described in this Example and by methods known to those of ordinary skill in the art.

EXAMPLE 35

A. *N*-(5-Chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-(2-nitro-1-methylthioethenyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide (0.185 g, 0.30 mmol) was dissolved in DMF (3 mL) under nitrogen. A 2.0 M solution of methylamine in THF (0.75 mL, 1.5 mmol) was added. The reaction mixture was stirred at ambient temperature for 16 hours, then poured into water (50 mL). The aqueous layer was extracted with ethyl acetate (3x30 mL). The combined organic layers were washed with water (3x40 mL), brine (40 mL), dried over magnesium sulfate, concentrated *in vacuo*, and dried under vacuum. Purification by HPLC on a C18 Dynamax column with acetonitrile in water gradient with 0.1% trifluoroacetic acid afforded *N*-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-(2-nitro-1-(methylamino)ethenyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt, as a mixture of geometric isomers; NMR (DMSO-d_6) 10.9 (d, 1), 9.6 (br, .5), 9.4 (s, 1), 8.8 (br, .5), 8.4 (d, 1), 8.1 (d, 1), 7.9 (dd, 1), 7.85 (s, 0.33), 7.75 (s, 0.33), 7.7 (s, 0.33), 7.4 (d, 1), 7.2 (d, 1), 6.2 (s, 1), 4.9 (s, .67), 4.7 (s, .67), 4.4 (s, .67), 3.9 (s, 3), 3.3 (s, 1), 3.2 (s, 1), 3.1 (d, 1), 3.0 (d, 1), 2.9 (d, 1), 2.8 (s, 1) ppm.

B. In a similar manner the following compound was made:

N-(5-chloropyridin-2-yl)-2-[((4-(*N'*-methyl-*N''*-(2-aminoethyl)-*N'''*-cyanoguanidino)methyl-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.4 (s, 1), 8.3 (s, 1), 8.1 (d, 1), 7.9 (dd, 1), 7.8 (br s, 2), 7.7 (s, 1), 7.3 (d, 2), 7.2 (s, 1), 4.6 (s, 2), 3.8 (s, 3), 3.5 (m, 2), 2.9 (br s, 5) ppm.

C. To a solution of *N*-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-(methylthio(cyanoimino)methyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide (0.1 g, 0.17 mmol) in DMF (10 mL) was added methylamine (0.84 mL of a 2 M solution in THF, 1.7 mmol). After stirring for 16 hours at ambient temperature, the reaction mixture was concentrated *in vacuo* to remove THF, poured into water and filtered. The resulting solid was purified by silica gel chromatography using 1-8% methanol in methylene chloride gradient followed by precipitation from CH_2Cl_2 and hexane to afford 0.072 g of *N*-(5-chloropyridin-2-yl)-2-[((4-(*N',N''*-dimethyl-*N'''*-cyanoguanidino)methyl-3-

chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, as a white solid; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.4 (s, 1), 8.3 (s, 1), 8.1 (d, 1), 7.9 (dd, 1), 7.6 (s, 1), 7.4 (s, 1), 7.3 (s, 1), 7.2 (br d, 1), 4.5 (s, 2), 3.8 (s, 3), 2.9 (d, 3), 2.85 (s, 3) ppm.

D. Other compounds of the invention may be prepared by methods similar to those described in this Example and by methods known to those of ordinary skill in the art.

EXAMPLE 36

A. Dimethylamine (40% aqueous, 0.51 mL, 4.1 mmol) was dissolved in DMF (2 mL) under nitrogen, and *N*-(5-chloropyridin-2-yl)-2-[((4-((5-trichloromethyl-1,2,4-oxadiazol-3-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide (0.151 g, 0.23 mmol) was added. The reaction mixture was stirred for 40 minutes at ambient temperature, then poured into water (40 mL). The aqueous layer was extracted with ethyl acetate (3x25 mL). The combined organic layers were washed with water (3x25 mL), brine (25 mL), dried over magnesium sulfate, concentrated *in vacuo*, and dried under vacuum. The crude product was purified by flash chromatography on silica gel, eluting with 75% ethyl acetate/ hexanes to afford *N*-(5-chloropyridin-2-yl)-2-[((4-((5-(dimethylamino)-1,2,4-oxadiazol-3-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide; NMR (DMSO-d_6) 10.9 (br, 1), 9.4 (br, 1), 8.4 (d, 1), 8.1 (d, 1), 7.9 (dd, 1), 7.8 (s, 1), 7.4 (d, 1), 7.2 (d, 1), 3.9 (s, 3), 3.8 (s, 2), 3.0 (s, 6) ppm.

B. In a similar manner, the following compound was prepared:
N-(5-chloropyridin-2-yl)-2-[((4-((5-amino-1,2,4-oxadiazol-3-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide; NMR (DMSO-d_6) 10.9 (s, 1), 9.4 (s, 1), 8.4 (d, 1), 8.1 (d, 1), 7.9 (dd, 1), 7.7 (s, 3), 7.4 (d, 1), 7.2 (d, 1), 3.9 (s, 3), 3.8 (s, 2) ppm.

C. Other compounds of the invention may be prepared by methods similar to those described in this Example and by methods known to those of ordinary skill in the art.

EXAMPLE 37

A. *N*-(4-chlorophenyl)-2-[(((4,5)-nitro-3-methylthiophen-2-yl)carbonyl)amino]-5-chlorobenzamide (1 g , 2.1 mmol) was stirred in a 4:1 ethanol/water solution (43 mL). To this solution was added iron (0.59 g, 10.6 mmol), and ammonium chloride (5.0 eq.) and the reaction mixture was refluxed for 1 hour. The reaction mixture was cooled to ambient temperature, filtered through Celite®, and the Celite® layer was washed with methylene chloride and ethyl acetate. The filtrate was washed with aqueous sodium bicarbonate, water and dried over

sodium sulfate to afford a rust-colored solid, 0.71 g (75% yield). Purification by flash chromatography on silica, eluting with 1:1 ethyl acetate/hexanes afforded *N*-(4-chlorophenyl)-2-[((5-amino-3-methylthiophen-2-yl)carbonyl)amino]-5-chlorobenzamide; NMR (DMSO-d_6/TFA) 10.7 (s, 1), 10.6 (s, 1), 8.4 (d, 1), 8.0 (s, 1), 7.8 (d, 2), 7.6 (d, 1), 7.4 (d, 2), 5.8 (s, 1) 2.4 (s, 3) ppm, and *N*-(4-chlorophenyl)-2-[((4-amino-3-methylthiophen-2-yl)carbonyl)amino]-5-chlorobenzamide.

B. To a solution of *N*-(4-chlorophenyl)-2-[((5-amino-3-methylthiophen-2-yl)carbonyl)amino]-5-chlorobenzamide (0.05 g, 0.114 mmol) in pyridine (3 mL) at 0°C was added acetyl chloride (0.009 mL, 0.125 mmol) and the reaction was warmed to ambient temperature. The reaction was stirred 3 hours and was poured into water and ice. The resulting solid was collected by filtration, washed with water and dried *in vacuo* to afford 0.03 g (55%) of *N*-(4-chlorophenyl)-2-[((5-acetamido-3-chlorothiophen-2-yl)carbonyl)amino]-5-chlorobenzamide; NMR (DMSO-d_6) 11.4 (s, 1), 10.8 (s, 1), 10.7 (s, 1), 8.3 (d, 1), 7.9 (s, 1), 7.8 (d, 2), 7.6 (d, 1), 7.4 (d, 2), 6.5 (s, 1), 2.4 (s, 3), 2.0 (d, 3) ppm.

C. Other compounds of the invention may be prepared by methods similar to those described in this Example and by methods known to those of ordinary skill in the art.

EXAMPLE 38

A. A suspension of *N*-(5-chloropyridin-2-yl)-2-[((4-(*N'*,*N''*-dimethyl-*N'''*-cyanoguanidino)methyl-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide (0.3 g, 0.52 mmol) in 3 M HCl (10 mL) was stirred for 24 hours at ambient temperature. The reaction mixture was made pH basic with 2 N NaOH and saturated aqueous $NaHCO_3$. The reaction mixture was filtered, and the solid was dissolved in methylene chloride. The solution was dried over Na_2SO_4, filtered, concentrated, and purified by flash chromatography on silica using 1-8% methanol in methylene chloride gradient followed by precipitation from CH_2Cl_2 and hexane to afford 0.115 g of *N*-(5-chloropyridin-2-yl)-2-[((4-(*N'*,*N''*-dimethyl-*N'''*-(aminocarbonyl)guanidino)methyl-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, as a white solid; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.4 (s, 1), 8.8 (br s, 1), 8.3 (s, 1), 8.1 (d, 1), 7.8 (m, 2), 7.3 (d, 2), 6.9 (br m, 1), 4.6 (s, 2), 3.8 (s, 3), 3.0 (s, 3), 2.9 (d, 3) ppm.

B. Other compounds of the invention may be prepared by methods similar to those described in this Example and by methods known to those of ordinary skill in the art.

EXAMPLE 39

A. To a solution of *N*-(5-chloropyridin-2-yl)-2-[((4-((*N'*-(2-aminoethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide (0.9 g, 1.7 mmol) in DMF (50 mL) was added excess of dimethyl *N*-cyanodithioimidocarbonate. After stirring for 16 hours at ambient temperature, the reaction mixture was concentrated *in vacuo*. Water was added, and the reaction mixture was extracted with methylene chloride. The combined extracts were dried over Na_2SO_4, filtered, concentrated, and purified by flash chromatography on silica using 1-8% methanol in methylene chloride to afford a white solid. The solid was dissolved in acetonitrile and heated at reflux for for 16 hours. The solution was concentrated and purified by HPLC on a C18 Dynamax column with 25-95% acetonitrile in water gradient with 0.1% trifluoroacetic acid to afford 0.084 g of *N*-(5-chloropyridin-2-yl)-2-[((4-((2-(cyanoimino)tetrahydroimidazol-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt, as a white solid; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.4 (s, 1), 8.4 (s, 1), 8.1 (d, 1), 8.0 (s, 1), 7.9 (dd, 1), 7.8 (s, 1), 7.4 (s, 1), 7.3 (s, 1), 4.3 (s, 2), 3.8 (s, 3), 3.4 (m, 4) ppm.

B. Other compounds of the invention may be prepared by methods similar to those described in this Example and by methods known to those of ordinary skill in the art.

EXAMPLE 40

A. To a solution of *N*-(4-chlorophenyl)-2-[((5-bromomethyl-3-chlorothiophen-2-yl)carbonyl)amino]-5-chlorobenzamide (0.3 g, 0.58 mmol) in dioxane (10 mL) and water (2 mL) was added $CaCO_3$ (0.29 g, 2.89 mmol). The resulting turbid solution was heated to reflux for 64 hours, and then cooled to ambient temperature. The reaction mixture was concentrated to remove dioxane and purified by flash chromatography on silica followed by precipitation from CH_2Cl_2 and hexane to afford 0.15 g of *N*-(4-chlorophenyl)-2-[((5-hydroxymethyl-3-chlorothiophen-2-yl)carbonyl)amino]-5-chlorobenzamide, as a yellow solid; NMR (DMSO-d_6/TFA) 11.1 (s, 1), 10.7 (s, 1), 8.4 (d, 1), 7.9 (s, 1), 7.7 (d, 2), 7.5 (d, 1), 7.3 (d, 2), 7.0 (s, 1), 4.6 (s, 2) ppm.

B. To a solution of *N*-(4-chlorophenyl)-2-[((5-hydroxymethyl-3-chlorothiophen-2-yl)carbonyl)amino]-5-chlorobenzamide (0.085 g, 0.19 mmol) in DMF (6 mL) was added pyridinium dichromate (PDC) (0.25 g, 0.65 mmol) at ambient temperature. After stirring for 20 hours, water was added and the reaction mixture was extracted with methylene chloride. The combined extracts were dried over Na_2SO_4, filtered, concentrated *in vacuo*, and purified by flash chromatography on silica to afford 0.035 g of *N*-(4-chlorophenyl)-2-[((5-formyl-3-

chlorothiophen-2-yl)carbonyl)amino]-5-chlorobenzamide, as a pale yellow solid; NMR (DMSO-d_6) 11.3 (s, 1), 10.8 (s, 1), 9.9 (s, 1), 8.3 (d, 1), 8.1 (s, 1), 7.9 (s, 1), 7.7 (d, 2), 7.6 (d, 1), 7.4 (d, 2) ppm.

C. To a solution of *N*-(4-chlorophenyl)-2-[((5-formyl-3-chlorothiophen-2-yl)carbonyl)amino]-5-chlorobenzamide (0.31 g, 0.69 mmol) in CCl_4 (10 mL) and benzene (15 mL) was added *N*-bromosuccinimide (NBS) (0.18 g, 1.03 mmol) and 2,2'-azobisisobutyronitrile (AIBN) (0.011 g, 0.068 mmol). The reaction mixture was heated to reflux for 1 hour, and the resulting clear yellow solution was cooled to 0°C. Methanol (0.1 mL) was added and the reaction mixture was stirred for 14 hours at ambient temperature. Water was added and the reaction mixture was extracted with methylene chloride. The combined extracts were dried over Na_2SO_4, filtered, concentrated *in vacuo*, and purified by flash chromatography on silica to afford 0.27 g of *N*-(4-chlorophenyl)-2-[((5-methoxycarbonyl-3-chlorothiophen-2-yl)carbonyl)amino]-5-chlorobenzamide. as a pale yellow solid; NMR (DMSO-d_6/TFA) 11.3 (s, 1), 10.8 (s, 1), 8.3 (d, 1), 7.9 (s, 1), 7.7 (m, 3), 7.6 (d, 1), 7.4 (d, 2), 3.8 (s, 3) ppm.

D. In a similar manner, the following compound was made:
N-(4-chlorophenyl)-2-[((5-(diethylamino)carbonyl-3-chlorothiophen-2-yl)carbonyl)amino]-5-chlorobenzamide; NMR ($CDCl_3$) 11.0 (s, 1), 9.2 (s, 1), 8.4 (d, 1), 7.7 (d, 2), 7.5 (s, 1), 7.4 (d, 1), 7.3 (d, 1), 7.2 (d, 1), 7.0 (s, 1), 3.5 (q, 4), 1.2 (t, 6) ppm.

E. Other compounds of the invention may be prepared by methods similar to those described in this Example and by methods known to those of ordinary skill in the art.

EXAMPLE 41

A. To a solution of *N*-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-oxazolin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide (5.0 g, 8.03 mmol) in ethanol (50 mL) at 40°C was added salicylic acid (1.22 g, 8.03 mmol) followed by the addition of ethyl acetate (125 mL). The solution was seeded with previously prepared crystals of the salicylic acid salt of *N*-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-oxazolin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide. Crystallization occurred as the solution cooled to ambient temperature. After 1 hour at ambient temperature the crystalline product was isolated by filtration. The solid was washed with ethyl acetate (50 mL), then dried *in vacuo* at 35°C for 24 hours to afford 5.4 g (87%) of the salicylic acid salt of *N*-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-oxazolin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, as a white solid. A vial was charged with salicylic acid salt of *N*-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-oxazolin-2-

yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide (200 mg). The vial was placed in an oil bath at 145°C to melt the solid then allowed to cool to ambient temperature to afford *N*-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N"*-(2-(((2-hydroxyphenyl)carbonyl)oxy)ethyl)ureido)-methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, in quantitative yield as an off-white solid; NMR (DMSO-d_6) 10.9 (s, 0.5), 10.5 (s, 0.5), 9.3 (s, 0.5), 8.4 (d, 1), 8.1 (d, 1), 7.9 (dd, 1), 7.8 (dd, 1), 7.5 (m, 2), 7.4 (d, 1) 7.3 (d, 1), 6.9 (m, 2), 6.7 (t, 1), 4.3 (m, 4), 3.9 (s, 3), 3.4 (d, 2), 3.3 (d, 4), 2.7 (s, 3) ppm.

B. In a similar manner, the following compound was made: *N*-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N"*-(2-(acetoxy)ethyl)ureido)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide; NMR (DMSO-d_6) 10.9 (s, 0.5), 9.3 (s, 0.5), 8.4 (s, 1), 8.1 (d, 1), 7.9 (dd, 1), 7.5 (s, 1), 7.4 (d, 1) 7.3 (d, 1), 6.6 (t, 1), 4.4 (s, 2), 4.0 (t, 2), 3.9 (s, 3), 3.4 (d, 2), 3.3 (m, 2), 2.8 (s, 3), 2.0 (s, 3) ppm.

C. Other compounds of the invention may be prepared by methods similar to those described in this Example and by methods known to those of ordinary skill in the art.

EXAMPLE 42

A. To a solution of *N*-(5-chloropyridin-2-yl)-2-[((4-((methylamino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide (0.70 g, 1.4 mmol) in THF (10 mL) at 0°C was added 2-bromoethylisocyanate (0.63 mL, 4.2 mmol) and the mixture stirred at ambient temperature. After 30 minutes, the mixture was cooled, concentrated *in vacuo* and the residue dissolved in DMF (4 mL). Pyrrolidine (0.50 g, 7.0 mmol) was added. The reaction was stirred for 1 hour and poured into water and ethyl acetate. The ethyl acetate layer was dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash chromatography on silica gel afforded 0.050 g of *N*-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N"*-(2-(pyrrolidin-1-yl)ethyl)ureido)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.6 (m, 1), 9.4 (s, 1), 8.3 (d, 1), 8.1 (d, 1), 7.9 (dd, 1), 7.5 (s, 1), 7.4 (s, 1), 7.3 (s, 1), 4.4 (s, 2), 3.9 (s, 3), 3.6 (m, 2), 3.4 (m, 2), 3.2 (m, 2), 3.0 (m, 2), 2.9 (s, 3), 2 (m, 2), 1.8 (m, 2) ppm.

B. Other compounds of the invention may be prepared by methods similar to those described in this Example and by methods known to those of ordinary skill in the art.

EXAMPLE 43

A. To a mixture of *N*-(5-chloropyridin-2-yl)-2-[((4-((2-iminotetrahydroimidazol-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide

(0.072 g, 1.3 mmol) and triethyl amine (0.13 g, 1.3 mmol) in dichloromethane (100 mL) was added methylchloroformate (0.12 g, 1.3 mmol) at 0°C. The reaction was allowed to warm and stirred at ambient temperature for 1 hour. The reaction was then quenched with methanol, and extracted between ethyl acetate and water. The ethyl acetate extract was purified by HPLC on a C18 Dynamax column with acetonitrile in water gradient with 0.1% trifluoroacetic acid to afford 0.12 g of *N*-(5-chloropyridin-2-yl)-2-[((4-((2-(methoxycarbonylamino)imidazolin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.5 (s., 1), 9.4 (s, 1), 8.3 (d, 2), 8.1 (d, 1), 7.9 (m, 2), 7.4 (d, 1), 7.3 (d, 1), 4.6 (s, 2), 3.9 (s, 3), 3.8 (s, 3), 3.6 (m, 4) ppm.

B. In a similar manner, to a mixture of *N*-(5-chloropyridin-2-yl)-2-[((4-((2-imino-tetrahydroimidazol-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide (0.56 g, 1.0 mmol) and triethyl amine (0.41 g, 3.0 mmol) in dichloromethane (100 mL) was added phenylisocyanate (0.36 g, 3.0 mmol) at 0°C. The reaction was allowed to warm and stirred at ambient temperature for 1 hour. The reaction was then quenched with methanol, and extracted between ethyl acetate and water. The ethyl acetate extract was purified by HPLC on a C18 Dynamax column with acetonitrile in water gradient with 0.1% trifluoroacetic acid to afford 0.12 g of *N*-(5-chloropyridin-2-yl)-2-[((4-((2-imino-3-((phenylamino)carbonyl)tetrahydroimidazol-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide, trifluoroacetic acid salt; NMR (DMSO-d_6/TFA) 10.9 (s, 1), 9.7 (s., 1), 9.6 (s, 1), 9.4 (s, 1), 8.3 (s, 1), 8.1 (d, 1), 7.9 (s, 1), 7.8 (dd, 1), 7.1~7.5 (m, 7), 4.6 (s, 2), 3.9 (s, 3), 3.6~3.8 (m, 4) ppm.

C. Other compounds of the invention may be prepared by methods similar to those described in this Example and by methods known to those of ordinary skill in the art.

EXAMPLE 44

A. 3-Methyl-2-formylbenzo[*b*]thiophene (0.68 g, 3.83 mmol) and *N'*-(4-chlorophenyl)-2-amino-5-benzamide (1.0 g, 3.83 mmol) were stirred at 0°C in acetic acid (20 mL) for 2 hours. Sodium cyanoborohydride (0.48 g, 7.64 mmol) was added and the reaction stirred for 16 hours at ambient temperature. The reaction was poured into water and the resulting pale yellow precipitate was collected by filtration. Purification by flash chromatography in ethyl acetate/hexanes afforded 0.14 g (10%) of *N'*-(4-chlorophenyl)-2-((3-methylbenzo[*b*]thien-2yl)methyl)amino-5-benzamide as a white solid; NMR ($CDCl_3$) 7.8 (s, 1), 7.7 (s, 1), 7.6 (s, 1), 7.5 (d, 2), 7.4 (m, 3), 7.2 (d, 2), 6.8 (d, 2), 4.6 (s, 2), 2.4 (s, 3), 2.3 (s, 3) ppm.

B. Other compounds of the invention may be prepared by methods similar to those described in this Example and by methods known to those of ordinary skill in the art.

EXAMPLE 45

A. To a solution of *N*-phenyl-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-4,5-dihydroxybenzamide (0.09 g, 0.21 mmol) in CH_2Cl_2 (1 mL) and pyridine (1 mL) at 0°C was added trimethylacetyl chloride (0.027 mL, 0.22 mmol). The solution was allowed to warm to ambient temperature with stirring. After 16 hours, the reaction mixture was partitioned between ethyl acetate and dilute HCl. The organic layer was dried over Na_2SO_4 and concentrated *in vacuo*. The resulting oil was purified by flash chromatography on silica gel to afford 0.038 g (40% yield) of *N*-phenyl-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-5-hydroxy-4-((1,1-dimethylethyl)carbonyl)oxybenzamide as a white solid; NMR(DMSO-d_6) 12.2 (s, 1), 10.8 (s, 1), 10.4 (s, 1), 8.3 (s, 1), 8.2 (d, 1), 8.0 (d, 1), 7.6-7.7 (m, 4), 7.4 (t, 2), 7.1 (t, 1), 1.3 (s, 9) ppm.

B. Other compounds of the invention may be prepared by methods similar to those described in this Example and by methods known to those of ordinary skill in the art.

EXAMPLE 46

This example illustrates the preparation of representative pharmaceutical compositions for oral administration containing a compound of the invention, or a pharmaceutically acceptable salt thereof, *e.g.*, *N*-(5-chloropyridin-2-yl)-2-[((4-((pyridinium-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-hydroxy-5-chlorobenzamide:

A.

Ingredients	% wt./wt.
Compound of the invention	20.0%
Lactose	79.5%
Magnesium stearate	0.5%

The above ingredients are mixed and dispensed into hard-shell gelatin capsules containing 100 mg each, one capsule would approximate a total daily dosage.

B.

Ingredients	% wt./wt.
Compound of the invention	20.0%
Magnesium stearate	0.9%
Starch	8.6%
Lactose	69.6%
PVP (polyvinylpyrrolidine)	0.9%

The above ingredients with the exception of the magnesium stearate are combined and

granulated using water as a granulating liquid. The formulation is then dried, mixed with the magnesium stearate and formed into tablets with an appropriate tableting machine.

C.

Ingredients	
Compound of the invention	0.1 g
Propylene glycol	20.0 g
Polyethylene glycol 400	20.0 g
Polysorbate 80	1.0 g
Water	q.s. 100 mL

The compound of the invention is dissolved in propylene glycol, polyethylene glycol 400 and polysorbate 80. A sufficient quantity of water is then added with stirring to provide 100 mL of the solution which is filtered and bottled.

D.

Ingredients	% wt./wt.
Compound of the invention	20.0%
Peanut Oil	78.0%
Span 60	2.0%

The above ingredients are melted, mixed and filled into soft elastic capsules.

E.

Ingredients	% wt./wt.
Compound of the invention	1.0%
Methyl or carboxymethyl cellulose	2.0%
0.9% saline	q.s. 100 mL

The compound of the invention is dissolved in the cellulose/saline solution, filtered and bottled for use.

EXAMPLE 47

This example illustrates the preparation of a representative pharmaceutical formulation for parenteral administration containing a compound of the invention, or a pharmaceutically acceptable salt thereof, *e.g.*, *N*-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N''*-ethylureido)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide:

Ingredients	
Compound of the invention	0.02 g
Propylene glycol	20.0 g
Polyethylene glycol 400	20.0 g
Polysorbate 80	1.0 g
0.9% Saline solution	q.s. 100 mL

The compound of the invention is dissolved in propylene glycol, polyethylene glycol 400

and polysorbate 80. A sufficient quantity of 0.9% saline solution is then added with stirring to provide 100 mL of the I.V. solution which is filtered through a 0.2 m membrane filter and packaged under sterile conditions.

EXAMPLE 48

This example illustrates the preparation of a representative pharmaceutical composition in suppository form containing a compound of the invention, or a pharmaceutically acceptable salt thereof, *e.g.*, *N*-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-5-methylbenzamide:

Ingredients	% wt./wt.
Compound of the invention	1.0%
Polyethylene glycol 1000	74.5%
Polyethylene glycol 4000	24.5%

The ingredients are melted together and mixed on a steam bath, and poured into molds containing 2.5 g total weight.

EXAMPLE 49

This example illustrates the preparation of a representative pharmaceutical formulation for insufflation containing a compound of the invention, or a pharmaceutically acceptable salt thereof, *e.g.*, *N*-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(2-(pyrrolidin-1-yl)ethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2-acetoxyethoxy)-5-chlorobenzamide:

Ingredients	% wt./wt.
Micronized compound of the invention	1.0%
Micronized lactose	99.0%

The ingredients are milled, mixed, and packaged in an insufflator equipped with a dosing pump.

EXAMPLE 50

This example illustrates the preparation of a representative pharmaceutical formulation in nebulized form containing a compound of the invention, or a pharmaceutically acceptable salt thereof, *e.g.*, *N*-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(dihydro-4(*H*)-1,3-oxazin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide:

Ingredients	% wt./wt.
Compound of the invention	0.005%
Water	89.995%
Ethanol	10.000%

The compound of the invention is dissolved in ethanol and blended with water. The formulation is then packaged in a nebulizer equipped with a dosing pump.

EXAMPLE 51

This example illustrates the preparation of a representative pharmaceutical formulation in aerosol form containing a compound of the invention, or a pharmaceutically acceptable salt thereof, *e.g.*, *N*-(4-chlorophenyl)-2-[((4-((*N'*-methyl-*N'*-(oxazolin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(morpholin-4-yl)-5-chlorobenzamide:

Ingredients	% wt./wt.
Compound of the invention	0.10%
Propellant 11/12	98.90%
Oleic acid	1.00%

The compound of the invention is dispersed in oleic acid and the propellants. The resulting mixture is then poured into an aerosol container fitted with a metering valve.

EXAMPLE 52

(*In vitro* assay for Factor Xa and Thrombin)

This assay demonstrates the activity of the compounds of the invention towards factor Xa, thrombin and tissue plasminogen activator. The activities were determined as an initial rate of cleavage of the peptide *p*-nitroanilide by the enzyme. The cleavage product, *p*-nitroaniline, absorbs at 405 nm with a molar extinction coefficient of 9920 $M^{-1}cm^{-1}$.

Reagents and Solutions:

Dimethyl sulfoxide (DMSO) (Baker analyzed grade).

Assay buffer:

50 mM TrisHCl, 150 mM NaCl, 2.5 mM $CaCl_2$, and

0.1% polyethylene glycol 6000, pH 7.5.

Enzymes (Enzyme Research Lab.):

1. Human factor Xa stock solution: 0.281 mg/mL in assay buffer, stored at -80°C (working solution (2X): 106 ng/mL or 2 nM in assay buffer, prepare prior to use).
2. Human thrombin stock solution: Concentration as specified by the supplier, stored at

-80°C (working solution (2X): 1200 ng/mL or 32 nM in assay buffer, prepare prior to use).

3. Human tissue plasminogen activator (tPA) (Two chains, Sigma or American Diagnostica Inc.) stock solution: Concentration as specified by the supplier, stored at -80°C (working solution (2X): 1361 ng/mL or 20 nM in assay buffer, prepare prior to use).

Chromogenic substrates (Pharmacia Hepar Inc.):

1. S2222 (FXa assay) stock solution: 6 mM in deionized H_20, store at 4°C (working solution (4X): 656 μM in assay buffer).
2. S2302 (Thrombin assay) stock solution: 10 mM in deionized H_2O, stored at 4°C (working solution (4X): 1200 μM in assay buffer).
3. S2288 (tPA assay) stock solution: 10 mM in deionized H_2O, stored at 4°C (working solution (4X): 1484 μM in assay buffer for Sigma tPA, or 1120 μM for American Diagnostica tPA).

Standard inhibitor compound stock solution:

5 mM in DMSO, stored at -20°C.

Test compounds (compounds of the invention) stock solutions:

10 mM in DMSO, stored at -20°C.

Assay procedure:

Assays were performed in 96-well microtiter plates in a total volume of 200 μl. Assay components were in final concentration of 50 mM TrisHCl, 150 mM NaCl, 2.5 mM $CaCl_2$, 0.1% polyethylene glycol 6000, pH 7.5, in the absence or presence of the standard inhibitor or the test compounds and enzyme and substrate at following concentrations: (1) 1 nM factor Xa (0.1nM or 0.2 nM factor Xa for compounds with K_iXa in low picomolar range) and 164 μM S2222; (2) 16 nM thrombin and 300 μM S2302; and (3) 10 nM tPA and 371 μM or 280 μM S2288. Concentrations of the standard inhibitor compound in the assay were from 5 μM to 0.021 μM in 1 to 3 dilution. Concentration of the test compounds in the assay typically were from 10 μM to 0.041 μM in 1 to 3 dilution. For potent test compounds, the concentrations used in the factor Xa assay were further diluted 100 fold (100 nM to 0.41 nM) or 1000 fold (10 nM to 0.041 nM). All substrate concentrations used are equal to their K_m values under the present assay conditions. Assays were performed at ambient temperature.

The first step in the assay was the preparation of 10 mM test compound stock solutions in DMSO (for potent test compounds, 10 mM stock solutions were further diluted to 0.1 or 0.01 μM for the factor Xa assay), followed by the preparation of test compound working

solutions (4X) by a serial dilutions of 10 mM stock solutions with Biomek 1000 in 96 deep well plates as follows:

(a) Prepare a 40 μM working solution by diluting the 10 mM stock 1 to 250 in assay buffer in 2 steps: 1 to 100, and 1 to 2.5.

(b) Make another five serial dilutions (1:3) of the 40 μM solution (600 μL for each concentration). A total of six diluted test compound solutions were used in the assay. Standard inhibitor compound (5 mM stock) or DMSO (control) went through the same dilution steps as those described above for test compounds.

The next step in the assay was to dispense 50 μL of the test compound working solutions (4X) (from 40 μM to 0.164 μM) in duplicate to microtiter plates with Biomek. To this was added 100 μL of enzyme working solution (2X) with Biomek. The resulting solutions were incubated at ambient temperature for 10 minutes.

To the solutions was added 50 μL of substrate working solution (4X) with Biomek.

The enzyme kinetics were measured at 405 nm at 10 seconds intervals for five minutes in a THERMOmax plate reader at ambient temperature. When a lower concentration of factor Xa was needed in the factor Xa assay, the enzyme kinetics were measured for fifteen minutes (0.2 nM factor Xa) or thirty minutes (0.1 nM factor Xa) at ambient temperature.

Calculation of K_i of the Test compounds:

Enzyme initial rates were calculated as mOD/min based on the first two minutes readings. The IC_{50} values were determined by fitting the data to the log-logit equation (linear) or the Morrison equation (non-linear) with an EXCEL spread-sheet. K_i values were then obtained by dividing the IC_{50} by 2. Routinely, K_i(factor Xa) values less than 3 nM were calculated from the Morrison equation.

Compounds of the invention, when tested in this assay, demonstrated the selective ability to inhibit human factor Xa and human thrombin.

EXAMPLE 53

(*In vitro* assay for Human Prothrombinase)

This assay demonstrates the ability of the compounds of the invention to inhibit prothrombinase. Prothrombinase (PTase) catalyzes the activation of prothrombin to yield fragment 1.2 plus thrombin with meizothrombin as the intermediate. This assay is an end point assay. Activity of the prothrombinase is measured by activity of thrombin (one of the reaction products) or by the amount of thrombin formed/time based on a thrombin standard curve (nM vs mOD/min). For determination of IC_{50} (PTase) of the compounds of the invention, PTase

activity was expressed by thrombin activity (mOD/min).

Materials:

Enzymes:

1. Human factor Va (Haematologic Technologies Inc., Cat# HCVA-0110) working solution: 1.0 mg/mL in 50% glycerol, 2 mM $CaCl_2$, stored at -20°C.
2. Human factor Xa (Enzyme Res. Lab. cat# HFXa1011) working solution: 0.281 mg/mL in assay buffer (without BSA), stored at -80°C.
3. Human prothrombin (FII) (Enzyme Res. Lab., Cat# HP1002) working solution: Diluted FII to 4.85 mg/mL in assay buffer (without BSA), stored at -80°C.

Phospholipid (PCPS) vesicles:

PCPS vesicles (80%PC, 20%PS) were prepared by modification of the method reported by Barenholz *et al.*, *Biochemistry* (1977), Vol. 16, pp. 2806-2810.

Phosphatidyl serine (Avanti Polar Lipids, Inc., Cat#840032):

10 mg/mL in chloroform, purified from brain, stored -20°C under nitrogen or argon.

Phosphatidyl Choline (Avanti Polar Lipids, Inc., Cat# 850457):

50 mg/ml in chloroform, synthetic 16:0-18:1 Palmitoyl-Oleoyl, stored at -20°C under nitrogen or argon.

Spectrozyme-TH (American Diagnostica Inc., Cat# 238L, 50 μmoles, stored at ambient temperature) working solution: Dissolved 50 μmoles in 10 mL dH_2O.

BSA (Sigma Chem Co., Cat# A-7888, FractionV, RIA grade).

Assay buffer: 50 mM TrisHCl, pH 7.5, 150 mM NaCl, 2.5 mM $CaCl_2$, 0.1% PEG 6000 (BDH), 0.05% BSA (Sigma, Fr.V, RIA grade).

For one plate assay, prepare the following working solutions:

1. Prothrombinase complex:

(a) 100 μM PCPS (27.5 μL of PCPS stock (4.36 mM) diluted to final 1200 μL with assay buffer.

(b) 25 nM Human factor Va: 5.08 μL of Va stock(1 mg/mL) was diluted to final 1200 μL with assay buffer.

(c) 5 pM Human factor Xa: Dilute factor Xa stock (0.281 mg/mL) 1:1,220,000 with assay buffer. Prepare at least 1200 μL.

Combine equal volumes (1100 μL) of each component in the order of PCPS, Va and Xa. Use immediately or store in ice (bring to ambient temperature before use).

2. 6 μM Human prothrombin (FII): dilute 124 μL of FII stock (4.85 mg/mL) to final 1400 μL with assay buffer.

3. 20 mM EDTA/Assay buffer: 0.8 mL of 0.5 M EDTA (pH 8.5) plus 19.2 mL assay buffer.
4. 0.2 mM Spectrozyme-TH/EDTA buffer: 0.44 mL of SPTH stock (5 mM) plus 10.56 mL of 20 mM EDTA/assay buffer.
5. Test compounds (compounds of the invention):

Prepare a working solution (5X) from 10 mM stock (DMSO) and make a series of 1:3 dilution. Compounds were assayed at 6 concentrations in duplicate.

Assay conditions and procedure:

Prothrombinase reaction was performed in final 50 μL of mixture containing PTase (20 μM PCPS, 5 nM hFVa, and 1 pM hFXa), 1.2 μM human factor II and varied concentration of the test compounds (5 μM to 0.021 μM or lower concentration range). Reaction was started by addition of PTase and incubated for 6 minutes at ambient temperature. Reaction was stopped by addition of EDTA/buffer to final 10 mM. Activity of thrombin (product) was then measured in the presence of 0.1 mM of Spectrozyme-TH as substrate at 405 nm for 5 minutes (10 seconds intervals) at ambient temperature in a THEROmax microplate reader. Reactions were performed in 96-well microtiter plates.

In the first step of the assay, 10 μL of diluted test compound (5X) or buffer was added to the plates in duplicate. Then 10 μL of prothrombin (hFII) (5X) was added to each well. Next 30 μL PTase was added to each well, mix for about 30 seconds. The plates were then incubated at ambient temperature for 6 minutes.

In the next step, 50 μL of 20 mM EDTA (in assay buffer) was added to each well to stop the reaction. The resulting solutions were then mixed for about 10 seconds. Then 100 μL of 0.2 mM spectrozyme was added to each well. The thrombin reaction rate was then measured at 405 nm for 5 minutes at 10 seconds intervals in a Molecular Devices microplate reader.

Calculations:

Thrombin reaction rate was expressed as mOD/min. using OD readings from the five minute reaction. IC_{50} values were calculated with the log-logit curve fit program.

The compounds of the invention demonstrated the ability to inhibit pro-thrombinase when tested in this assay.

EXAMPLE 54

(*In vivo* assay)

The following assay demonstrates the ability of the compounds to act as anti-coagulants.

Male rats (250-330 g) were anesthetized with sodium pentobarbital (90 mg/kg, i.p.) and

prepared for surgery. The left carotid artery was cannulated for the measurement of blood pressure as well as for taking blood samples to monitor clotting variables (prothrombin time (PT) and activated partial thromboplastin time (aPTT)). The tail vein was cannulated for the purpose of administering the test compounds (*i.e.*, the compounds of the invention and standards) and the thromboplastin infusion. The abdomen was opened *via* a mid-line incision and the abdominal vena cava was isolated for 2-3 cm distal to the renal vein. All venous branches in this 2-3 cm segment of the abdominal vena cava were ligated. Following all surgery, the animals were allowed to stabilize prior to beginning the experiment. Test compounds were administered as an intravenous bolus (t=0). Three minutes later (t=3), a 5-minute infusion of thromboplastin was begun. Two minutes into the infusion (t=5), the abdominal vena cava was ligated at both the proximal and distal ends. The vessel was left in place for 60 minutes, after which it was excised from the animal, slit open, the clot (if any) carefully removed, and weighed. Statistical analysis on the results was performed using a Wilcoxin-matched-pairs signed rank test.

The compounds of the invention, when tested in this assay, demonstrated the ability to inhibit the clotting of the blood.

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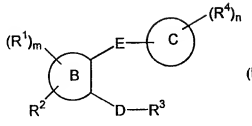
While the present invention has been described with reference to the specific embodiments thereof, it should be understood by those skilled in the art that various changes may be made and equivalents may be substituted without departing from the true spirit and scope of the invention. In addition, many modifications may be made to adapt a particular situation, material, composition of matter, process, process step or steps, to the objective, spirit and scope of the present invention. All such modifications are intended to be within the scope of the claims appended hereto.

WHAT IS CLAIMED IS:

1. A compound of the formula (III):

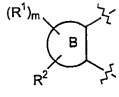


(III)

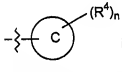
wherein

m is 1 to 3;

n is 1 to 5;



is an aryl or a heterocyclic ring substituted by R^2 and one or more R^1 groups;



is an aryl or a heterocyclic ring substituted by one or more R^4 groups;

D and E are independently a linker selected from the group consisting of $-N(R^5)-C(X)-$; $-R^8-N(R^5)-C(X)-$; $-N(R^5)-C(X)-R^8-$; $-R^8-N(R^5)-C(X)-R^8-$; $-N(R^5)-S(O)_p-$; $-R^8-N(R^5)-S(O)_p-$; $-N(R^5)-S(O)_p-R^8-$; and $-R^8-N(R^5)-S(O)_p-R^8-$ (where p is 0 to 2; X is oxygen, sulfur or H_2) where D and E can be attached to the B ring having the R^1 and R^2 substituents by either terminus of the linker;

each R^1 is independently hydrogen, alkyl, aryl, aralkyl, halo, haloalkyl, cyano, $-OR^5$, $-S(O)_p-R^9$ (where p is 0 to 2), $-C(O)OR^5$, $-C(O)N(R^5)R^6$, $-N(R^5)R^6$, $-O-C(O)R^5$, $-N(R^5)-CH(R^{12})-C(O)OR^5$, heterocyclyl (optionally substituted by alkyl, aryl, aralkyl, halo, haloalkyl, oxo, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ or $-C(O)N(R^5)R^6$) or heterocyclylalkyl (optionally substituted by alkyl, aryl, aralkyl, halo, haloalkyl, oxo, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ or $-C(O)N(R^5)R^6$);

R^2 is hydrogen, alkyl, aryl, aralkyl, halo, haloalkyl, cyano, $-OR^5$, $-S(O)_p-R^9$ (where p is 0 to 2), $-C(O)OR^5$, $-C(O)N(R^5)R^6$, $-N(R^{10})R^{11}$, $-C(R^7)H-N(R^{10})R^{11}$, $-C(R^7)H-R^8-N(R^{10})R^{11}$, $-C(R^7)H-OR^5$, $-C(R^7)H-R^8-OR^5$, $-C(R^7)H-S(O)_p-R^9$ (where p is 0 to 2), $-C(R^7)H-R^8-S(O)_p-R^9$

(where p is 0 to 2), $-O-R^8-S(O)_p-R^9$ (where p is 0 to 2), $-C(R^7)H-N(R^5)R^6$, $-C(R^7)H-R^8-N(R^5)R^6$, $-O-R^8-CH(OH)-CH_2-N(R^{10})R^{11}$, $-O-R^8-N(R^{10})R^{11}$, $-O-R^8-O-C(O)R^5$, $-O-R^8-CH(OH)-CH_2-OR^5$, $-O-(R^8-O)_t-R^5$ (where t is 1 to 6), $-O-(R^8-O)_t-R^{19}$ (where t is 1 to 6), $-O-R^8-C(O)R^5$, $-O-R^8-C(O)R^{19}$, $-O-R^8-C(O)OR^5$, $-N(R^5)-R^8-N(R^{10})R^{11}$, $-S(O)_p-R^8-N(R^5)R^6$ (where p is 0 to 2), $-S(O)_p-R^8-C(O)OR^5$ (where p is 0 to 2), or $-N(R^5)-CH(R^{12})-C(O)OR^5$;

R^3 is aryl or heterocyclyl both substituted by one or more R^{14} substituents independently selected from the group consisting of hydrogen, alkyl, halo, formyl, acetyl, cyano, $-R^8-CN$, $-N(R^{10})R^{11}$, $-R^8-N(R^{10})R^{11}$, $-R^8-N^{\oplus}(R^9)(R^{16})_2$, $-C(O)OR^5$, $-R^8-C(O)OR^5$, $-OR^5$, $-R^8-OR^5$, $-C(R^7)H-O-R^{15}$, $-S(O)_p-R^{15}$ (where p is 0 to 2), $-R^8-S(O)_p-R^{15}$ (where p is 0 to 2), $-S(O)_p-N(R^5)R^6$ (where p is 0 to 2), $-C(O)N(R^5)R^6$, $-R^8-C(O)N(R^5)R^6$, $-N(R^5)-(R^8-O)_t-R^5$ (where t is 1 to 6), $-R^8-N(R^5)-(R^8-O)_t-R^5$ (where t is 1 to 6), $-R^8-O-(R^8-O)_t-R^5$ (where t is 1 to 6), $-O-R^8-CH(OH)-CH_2-OR^5$, $-C(R^7)H-O-R^8-CH(OH)-CH_2-OR^5$, $-C(R^7)H-N(R^5)-R^8-[CH(OH)]_t-CH_2-OR^5$ (where t is 1 to 6), $-C(R^7)H-N(R^5)-S(O)_2-N(R^{10})R^{11}$, $-C(R^7)H-N(R^{10})-C(NR^{17})-N(R^{10})R^{11}$, $-C(R^7)H-N(R^{10})-C(NR^{17})-R^{10}$, $-C(NR^{17})-N(R^5)R^6$, $-C(R^7)H-C(NR^{17})-N(R^5)R^6$, $-C(R^7)H-O-N(R^5)R^6$, heterocyclyl (wherein the heterocyclyl radical is not attached to the rest of the molecule through a nitrogen atom and is optionally substituted by alkyl, aryl, aralkyl, halo, haloalkyl, oxo, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ or $-C(O)N(R^5)R^6$), and heterocyclylalkyl (wherein the heterocyclyl radical is not attached to the alkyl radical through a nitrogen ring and is optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, oxo, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ and $-C(O)N(R^5)R^6$);

each R^4 is independently hydrogen, alkyl, halo, haloalkyl, cyano, nitro, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$, $-C(O)N(R^5)R^6$, or $-R^8-N(R^5)R^6$;

each R^5 and R^6 is independently hydrogen, alkyl, aryl or aralkyl;

each R^7 is independently hydrogen or alkyl;

each R^8 is independently a straight or branched alkylene, alkylidene or alkylidyne chain;

each R^9 is independently alkyl, aryl or aralkyl;

each R^{10} and R^{11} is independently hydrogen, alkyl, haloalkyl, aryl, aralkyl, formyl, cyano, $-R^8-CN$, $-OR^5$, $-R^8-OR^5$, $-S(O)_p-R^{15}$ (where p is 0 to 2), $-R^8-S(O)_p-R^{15}$ (where p is 0 to 2), $-N(R^5)R^6$, $-R^8-N(R^5)R^6$, $-R^8-C(O)OR^5$, $-C(O)-R^{15}$, $-C(O)NH_2$, $-R^8-C(O)NH_2$, $-C(S)NH_2$, $-C(O)-S-R^5$, $-C(O)-N(R^5)R^{15}$, $-R^8-C(O)-N(R^5)R^{15}$, $-C(S)-N(R^5)R^{15}$, $-R^8-N(R^5)-C(O)H$, $-R^8-N(R^5)-C(O)R^{15}$, $-C(O)O-R^8-N(R^5)R^6$, $-C(N(R^5)R^6)=C(R^{18})R^{10}$, $-R^8-N(R^5)-P(O)(OR^5)_2$, cycloalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, halo

and -OR^5), heterocyclyl (optionally substituted by alkyl, aryl, aralkyl, halo, haloalkyl, oxo, -OR^5, -R^8-OR^5, -C(O)OR^5, -$S(O)_p$-R^9 (where p is 0 to 2), -R^8-$S(O)_p$-R^9 (where p is 0 to 2), -$N(R^5)R^6$ or -C(O)$N(R^5)R^6$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, oxo, -OR^5, -R^8-OR^5, -C(O)OR^5, -$S(O)_p$-R^9 (where p is 0 to 2), -R^8-$S(O)_p$-R^9 (where p is 0 to 2), -$N(R^5)R^6$ and -C(O)$N(R^5)R^6$);

or R^{10} and R^{11} together with the nitrogen to which they are attached form a *N*-heterocyclic ring containing zero to three additional hetero atoms, where the *N*-heterocylic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, halo, haloalkyl, aryl, aralkyl, oxo, nitro, cyano, -R^8-CN, =$N(R^{17})$, -OR^5, -C(O)OR^5, -R^8-C(O)OR^5, -$N(R^5)R^6$, -R^8-$N(R^5)R^6$, -C(O)$N(R^5)R^6$, -R^8-C(O)$N(R^5)R^6$, -$N(R^5)$-$N(R^5)R^6$, -C(O)R^5, -C(O)-(R^8-O)$_t$-R^5 (where t is 1 to 6), -$S(O)_p$-R^9 (where p is 0 to 2), -R^8-$S(O)_p$-R^8 (where p is 0 to 2), -(R^8-O)$_t$-R^5 (where t is 1 to 6), and heterocyclyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, -OR^5, -C(O)OR^5, -$N(R^5)R^6$, and -C(O)$N(R^5)R^6$);

R^{12} is a side chain of an α-amino acid;

each R^{15} is independently alkyl, cycloalkyl, haloalkyl, aryl, aralkyl, -R^8-O-C(O)-R^5, -R^8-OR^5, -$N(R^5)R^6$, -R^8-$N(R^5)R^6$, -R^8-C(O)OR^5, heterocyclyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, -OR^5, -R^8-OR^5, -C(O)OR^5, -$N(R^5)R^6$, and -C(O)$N(R^5)R^6$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, -OR^5, -R^8-OR^5, -C(O)OR^5, -$N(R^5)R^6$, and -C(O)$N(R^5)R^6$);

or R^5 and R^{15} together with the nitrogen to which they are attached form a *N*-heterocyclic ring containing zero to three additional hetero atoms, where the *N*-heterocyclic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, amino, monoalkylamino, dialkylamino, OR^5, -C(O)OR^5, aminocarbonyl, monoalkylaminocarbonyl, and dialkylaminocarbonyl;

each R^{16} is independently alkyl, aryl, aralkyl, -R^8-OR^5, -R^8-$N(R^5)R^6$, cycloalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, halo and -OR^5), heterocyclyl (optionally substituted by alkyl, aryl, aralkyl, halo, haloalkyl, -OR^5, -C(O)OR^5, -$N(R^5)R^6$ or -C(O)$N(R^5)R^6$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, -OR^5, -C(O)OR^5, -$N(R^5)R^6$ and -C(O)$N(R^5)R^6$); or

both R^{16}'s together with the nitrogen to which they are attached (and wherein the R^9 substituent is not present) form an aromatic *N*-heterocyclic ring containing zero to three additional

hetero atoms, where the *N*-heterocylic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-R^8-C(O)OR^5$, $-N(R^5)R^6$, $-R^8-N(R^5)R^6$, $-C(O)R^5$, $-C(O)-(R^8-O)_t-R^5$ (where t is 1 to 6), and $-(R^8-O)_t-R^5$ (where t is 1 to 6);

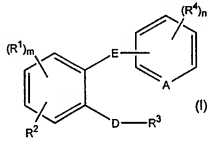
each R^{17} is independently hydrogen, alkyl, aryl, aralkyl, cyano, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-R^8-C(O)OR^5$, $-C(O)-N(R^5)R^8$, or $-R^8-C(O)-N(R^5)R^6$;

R^{18} is hydrogen, alkyl, aryl, aralkyl, cyano, $-C(O)OR^5$, or $-NO_2$; and

each R^{19} is cycloalkyl, haloalkyl, $-R^8-OR^5$, $-R^8-N(R^5)R^6$, $-R^8-C(O)OR^5$, $-R^8-C(O)N(R^5)R^8$, heterocyclyl (optionally substituted by alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ or $-C(O)N(R^5)R^6$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ and $-C(O)N(R^5)R^6$);

as a single stereoisomer or a mixture thereof; or a pharmaceutically acceptable salt thereof.

2. The compound of Claim 1 selected from formula (I):



(I)

A is =CH- or =N-;

m is 1 to 3;

n is 1 to 4;

D is $-N(R^5)-C(Z)-$ or $-N(R^5)-S(O)_p-$ (where p is 0 to 2; Z is oxygen, sulfur or H_2; and the nitrogen atom is directly bonded to the phenyl ring having the R^1 and R^2 substituents);

E is $-C(Z)-N(R^5)-$ or $-S(O)_p-N(R^5)-$ (where p is 0 to 2; Z is oxygen, sulfur or H_2; and the nitrogen atom can be bonded to the phenyl ring having the R^1 and the R^2 substituents or to the aromatic ring having the R^4 substituent);

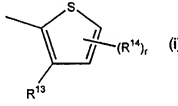
each R^1 is independently hydrogen, alkyl, aryl, aralkyl, halo, haloalkyl, cyano, $-OR^5$, $-S(O)_p-R^9$ (where p is 0 to 2), $-C(O)OR^5$, $-C(O)N(R^5)R^6$, $-N(R^5)R^6$, $-O-C(O)R^5$, or $-N(R^5)-CH(R^{12})-C(O)OR^5$;

or two adjacent R^1's together with the carbons to which they are attached form a heterocyclic ring

fused to the phenyl ring wherein the heterocyclic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl and aralkyl;

R^2 is hydrogen, alkyl, aryl, aralkyl, halo, haloalkyl, cyano, $-OR^5$, $-S(O)_p-R^9$ (where p is 0 to 2), $-C(O)OR^5$, $-OC(O)-R^5$, $-C(O)N(R^5)R^6$, $-N(R^{10})R^{11}$, $-C(R^7)H-N(R^{10})R^{11}$, $-C(R^7)H-R^8-N(R^{10})R^{11}$, $-C(R^7)H-OR^5$, $-C(R^7)H-R^8-OR^5$, $-C(R^7)H-S(O)_p-R^9$ (where p is 0 to 2), $-C(R^7)H-R^8-S(O)_p-R^9$ (where p is 0 to 2), $-O-R^8-S(O)_p-R^9$ (where p is 0 to 2), $-C(R^7)H-N(R^5)R^6$, $-C(R^7)H-R^8-N(R^5)R^8$, $-O-R^8-CH(OH)-CH_2-N(R^{10})R^{11}$, $-O-R^8-N(R^{10})R^{11}$, $-O-R^8-O-C(O)R^5$, $-O-R^8-CH(OH)-CH_2-OR^5$, $-O-(R^8-O)_t-R^5$ (where t is 1 to 6), $-O-(R^8-O)_t-R^{19}$ (where t is 1 to 6), $-O-R^8-C(O)R^5$, $-O-R^8-C(O)R^{19}$, $-O-R^8-C(O)OR^5$, $-N(R^5)-R^8-N(R^{10})R^{11}$, $-S(O)_p-R^8-N(R^5)R^6$ (where p is 0 to 2), $-S(O)_p-R^8-C(O)OR^5$ (where p is 0 to 2), or $-N(R^5)-CH(R^{12})-C(O)OR^5$;

R^3 is a radical of formula (i):



(i)

where:

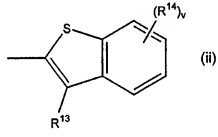
r is 1 or 2;

R^{13} is hydrogen, alkyl, halo, haloalkyl, $-N(R^5)R^6$, $-C(R^7)H-N(R^5)R^6$, $-OR^5$, $-R^8-OR^5$, $-S(O)_p-R^8-N(R^5)R^6$ (where p is 0 to 2) or heterocyclylalkyl (where the heterocyclic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, halo, aralkyl, nitro and cyano); and

each R^{14} is independently hydrogen, alkyl, halo, formyl, acetyl, cyano, $-R^8-CN$, $-N(R^{10})R^{11}$, $-C(R^7)H-N(R^{10})R^{11}$, $-C(R^7)H-R^8-N(R^{10})R^{11}$, $-C(R^7)H-N^{\oplus}(R^9)(R^{16})_2$, $-C(R^7)H-R^8-N^{\oplus}(R^9)(R^{16})_2$, $-C(O)OR^5$, $-C(R^7)H-C(O)OR^5$, $-C(R^7)H-R^8-C(O)OR^5$, $-OR^5$, $-C(R^7)H-OR^5$, $-C(R^7)H-R^8-OR^5$, $-C(R^7)H-O-R^{15}$, $-S(O)_p-R^{15}$ (where p is 0 to 2), $-C(R^7)H-S(O)_p-R^{15}$ (where p is 0 to 2), $-C(R^7)H-R^8-S(O)_p-R^{15}$ (where p is 0 to 2), $-S(O)_p-N(R^5)R^6$ (where p is 0 to 2), $-C(O)N(R^5)R^6$, $-C(R^7)H-C(O)N(R^5)R^6$, $-C(R^7)H-R^8-C(O)N(R^5)R^6$, $-C(R^7)H-N(R^5)-(R^8-O)_t-R^5$ (where t is 1 to 6), $-C(R^7)H-R^8-N(R^5)-(R^8-O)_t-R^5$ (where t is 1 to 6), $-C(R^7)H-O-(R^8-O)_t-R^5$ (where t is 1 to 6), $-C(R^7)H-R^8-O-(R^8-O)_t-R^5$ (where t is 1 to 6), $-O-R^8-CH(OH)-CH_2-OR^5$, $-C(R^7)H-O-R^8-CH(OH)-CH_2-OR^5$, $-C(R^7)H-N(R^5)-R^8-[CH(OH)]_t-CH_2-OR^5$ (where t is

1 to 6), $-C(R^7)H-N(R^5)-S(O)_2-N(R^{10})R^{11}$, $-C(R^7)H-N(R^{10})-C(NR^{17})-N(R^{10})R^{11}$, $-C(R^7)H-N(R^{10})-C(NR^{17})-R^{10}$, $-C(NR^{17})-N(R^5)R^6$, $-C(R^7)H-C(NR^{17})-N(R^5)R^6$, $-C(R^7)H-O-N(R^5)R^6$, heterocyclyl (wherein the heterocyclyl radical is not attached to the radical of formula (i) through a nitrogen atom and is optionally substituted by alkyl, aryl, aralkyl, halo, haloalkyl, oxo, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ or $-C(O)N(R^5)R^6$), or heterocyclylalkyl (wherein the heterocyclyl radical is not attached to the alkyl radical through a nitrogen atom and is optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, oxo, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ and $-C(O)N(R^5)R^6$);

or R^3 is a radical of the formula (ii):



(ii)

where v is 1 to 4;

R^{13} is as defined above for formula (i); and

R^{14} is as defined above for formula (i);

each R^4 is independently hydrogen, alkyl, halo, haloalkyl, cyano, nitro, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$, $-C(O)N(R^5)R^6$, or $-R^8-N(R^5)R^6$;

R^5 and R^6 are each independently hydrogen, alkyl, aryl or aralkyl;

each R^7 is independently hydrogen or alkyl;

each R^8 is independently a straight or branched alkylene, alkylidene or alkylidyne chain;

each R^9 is independently alkyl, aryl or aralkyl;

R^{10} and R^{11} are each independently hydrogen, alkyl, haloalkyl, aryl, aralkyl, formyl, cyano, $-R^8-CN$, $-OR^5$, $-R^8-OR^5$, $-S(O)_p-R^{15}$ (where p is 0 to 2), $-R^8-S(O)_p-R^{15}$ (where p is 0 to 2), $-N(R^5)R^6$, $-R^8-N(R^5)R^6$, $-R^8-C(O)OR^5$, $-C(O)-R^{15}$, $-C(O)NH_2$, $-R^8-C(O)NH_2$, $-C(S)NH_2$, $-C(O)-S-R^5$, $-C(O)-N(R^5)R^{15}$, $-R^8-C(O)-N(R^5)R^{15}$, $-C(S)-N(R^5)R^{15}$, $-R^8-N(R^5)-C(O)H$, $-R^8-N(R^5)-C(O)R^{15}$, $-C(O)O-R^8-N(R^5)R^6$, $-C(N(R^5)R^6)=C(R^{18})R^{10}$, $-R^8-N(R^5)-P(O)(OR^5)_2$, cycloalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, halo and $-OR^5$), heterocyclyl (optionally substituted by alkyl, aryl, aralkyl, halo, haloalkyl, oxo, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-S(O)_p-R^9$ (where p is 0 to 2), $-R^8-S(O)_p-R^9$ (where p is 0 to 2),

$-N(R^5)R^6$ or $-C(O)N(R^5)R^6$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, oxo, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-S(O)_p-R^9$ (where p is 0 to 2), $-R^8-S(O)_p-R^9$ (where p is 0 to 2), $-N(R^5)R^6$ and $-C(O)N(R^5)R^6$);

or R^{10} and R^{11} together with the nitrogen to which they are attached form a *N*-heterocyclic ring containing zero to three additional hetero atoms, where the *N*-heterocylic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, halo, haloalkyl, aryl, aralkyl, oxo, nitro, cyano, $-R^8-CN$, $=N(R^{17})$, $-OR^5$, $-C(O)OR^5$, $-R^8-C(O)OR^5$, $-N(R^5)R^6$, $-R^8-N(R^5)R^6$, $-C(O)N(R^5)R^6$, $-R^8-C(O)N(R^5)R^6$, $-N(R^5)-N(R^5)R^6$, $-C(O)R^5$, $-C(O)-(R^8-O)_t-R^5$ (where t is 1 to 6), $-S(O)_p-R^9$ (where p is 0 to 2), $-R^8-S(O)_p-R^9$ (where p is 0 to 2), $-(R^8-O)_t-R^5$ (where t is 1 to 6), and heterocyclyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$, and $-C(O)N(R^5)R^6$);

R^{12} is a side chain of an α-amino acid;

each R^{15} is independently alkyl, cycloalkyl, haloalkyl, aryl, aralkyl, $-R^8-O-C(O)-R^5$, $-R^8-OR^5$, $-N(R^5)R^6$, $-R^8-N(R^5)R^6$, $-R^8-C(O)OR^5$, heterocyclyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$, and $-C(O)N(R^5)R^6$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$, and $-C(O)N(R^5)R^6$);

or R^5 and R^{15} together with the nitrogen to which they are attached form a *N*-heterocyclic ring containing zero to three additional hetero atoms, where the *N*-heterocyclic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, amino, monoalkylamino, dialkylamino, $-OR^5$, $-C(O)OR^5$, aminocarbonyl, monoalkylaminocarbonyl, and dialkylaminocarbonyl;

each R^{16} is independently alkyl, aryl, aralkyl, $-R^8-OR^5$, $-R^8-N(R^5)R^6$, cycloalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, halo and $-OR^5$), heterocyclyl (optionally substituted by alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ or $-C(O)N(R^5)R^6$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ and $-C(O)N(R^5)R^6$); or

both R^{16}'s together with the nitrogen to which they are attached (and wherein the R^9 substituent is not present) form an aromatic *N*-heterocyclic ring containing zero to three additional hetero atoms, where the *N*-heterocylic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, $-OR^5$, $-C(O)OR^5$,

$-R^8-C(O)OR^5$, $-N(R^5)R^6$, $-R^8-N(R^5)R^6$, $-C(O)R^5$, $-C(O)-(R^8-O)_t-R^5$ (where t is 1 to 6), and $-(R^8-O)_t-R^5$ (where t is 1 to 6);

each R^{17} is independently hydrogen, alkyl, aryl, aralkyl, cyano, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-R^8-C(O)OR^5$, $-C(O)-N(R^5)R^6$, or $-R^8-C(O)-N(R^5)R^6$;

R^{18} is hydrogen, alkyl, aryl, aralkyl, cyano, $-C(O)OR^5$, or $-NO_2$; and

each R^{19} is cycloalkyl, haloalkyl, $-R^8-OR^5$, $-R^8-N(R^5)R^6$, $-R^8-C(O)OR^5$, $-R^8-C(O)N(R^5)R^6$, heterocyclyl (optionally substituted by alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ or $-C(O)N(R^5)R^6$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ and $-C(O)N(R^5)R^6$);

as a single stereoisomer or a mixture thereof; or a pharmaceutically acceptable salt thereof; provided that when A is =CH-, m is 1, n is 1, D is -N(H)-C(O)- (where the nitrogen atom is directly bonded to the phenyl ring having the R^1 and R^2 substituents), E is -C(O)-N(H)- (where the nitrogen atom is directly bonded to the phenyl ring having the R^4 substitutent), R^1 is hydrogen and R^2 is in the 5-position and is methyl, R^4 is in the 4-position and is fluoro, R^3 can not be a radical of formula (ii) where v is 1, R^{14} is hydrogen, and R^{13} is chloro.

3. The compound of Claim 2 wherein:

A is =N-;

m is 1 to 3;

n is 1 to 4;

D is $-N(R^5)-C(Z)-$ (where Z is oxygen, sulfur or H_2, and R^5 is hydrogen or alkyl);

E is $-C(Z)-N(R^5)-$ (where Z is oxygen, sulfur or H_2, R^5 is hydrogen or alkyl, and the nitrogen is attached to the pyridinyl ring);

R^1 is halo or haloalkyl;

R^2 is $-N(R^{10})R^{11}$, $-O-R^8-S(O)_p-R^9$ (where p is 0), $-O-R^8-C(O)OR^5$, $-O-(R^8-O)_t-R^5$ (where t is 1) or $-O-R^8-N(R^{10})R^{11}$ where:

each R^5 is independently hydrogen or alkyl;

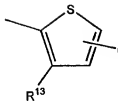
each R^8 is independently a straight or branched alkylene chain;

R^9 is alkyl; and

R^{10} and R^{11} are each independently hydrogen, alkyl, or $-R^8-O-R^5$ (where R^8 is a straight or branched alkylene chain and R^5 is hydrogen or alkyl);

or R^{10} and R^{11} together with the nitrogen to which they are attached form a *N*-heterocyclic ring containing zero to one additional hetero atoms, where the *N*-heterocyclic ring is optionally substituted by alkyl;

R^3 is a radical of the formula (i):



(i)

where r is 1;

R^{13} is halo; and

R^{14} is $-C(R^7)H-N(R^{10})R^{11}$ where:

R^7 is hydrogen; and

R^{10} and R^{11} together with the nitrogen to which they are attached form piperazinyl optionally substituted by one or more substituents selected from the group consisting of alkyl and $-C(O)R^5$; and

R^4 is hydrogen or halo.

4. The compound of Claim 3 wherein:

m is 1;

n is 1;

D is -N(H)-C(O)-;

E is -C(O)-N(H)- (where the nitrogen is bonded to the 2-position of the pyridinyl ring);

R^1 is halo in the 5-position;

R^2 is $-N(R^{10})R^{11}$, $-O-R^8-S(O)_p-R^9$ (where p is 0), $-O-R^8-C(O)OR^5$, $-O-(R^8-O)_t-R^5$ (where t is 1) or $-O-R^8-N(R^{10})R^{11}$ where:

each R^5 is independently hydrogen, methyl or ethyl;

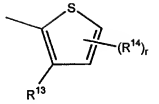
each R^8 is independently a methylene, ethylene or propylene chain;

R^9 is methyl or ethyl; and

R^{10} and R^{11} are each independently hydrogen, methyl, ethyl, or $-R^8-O-R^5$ (where R^8 is ethylene and R^5 is hydrogen, methyl or ethyl); or

R^{10} and R^{11} together with the nitrogen to which they are attached form a *N*-heterocyclic ring containing zero to one additional hetero atoms, where the *N*-heterocyclic ring is optionally substituted by alkyl;

R^3 is a radical of the formula (i):



(i)

where r is 1;

R^{13} is chloro; and

R^{14} is in the 4-position and is $-C(R^7)H-N(R^{10})R^{11}$ where:

R^7 is hydrogen; and

R^{10} and R^{11} together with the nitrogen to which they are attached form piperazinyl optionally substituted by methyl or ethyl; and

R^4 is hydrogen, bromo or chloro in the 5-position.

5. The compound of Claim 4 wherein:

R^1 is chloro;

R^2 is $-O-R^8-S(O)_p-R^9$ (where p is 0), $-O-R^8-C(O)OR^5$ or $-O-(R^8-O)_t-R^5$ (where t is 1 or 2) where:

each R^5 is independently hydrogen, methyl or ethyl;

each R^8 is independently a methylene, ethylene or propylene chain; and

R^9 is methyl or ethyl.

6. The compound of Claim 5 which is selected from the group consisting of:

N-(5-chloropyridin-2-yl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(methylthio)methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(ethoxycarbonyl)methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2-hydroxyethoxy)-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2-methoxyethoxy)-5-chlorobenzamide; and

N-(5-chloropyridin-2-yl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2-ethoxyethoxy)-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((4-ethylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2-methoxyethoxy)-5-chlorobenzamide, and

N-(5-chloropyridin-2-yl)-2-[((4-((4-ethylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2-(2-methoxyethoxy)ethoxy)-5-chlorobenzamide.

7. The compound of Claim 4 wherein

R^1 is chloro; and

R^2 is $-N(R^{10})R^{11}$ or $-O-R^8-N(R^{10})R^{11}$ where:

R^8 is a methylene, ethylene or propylene chain; and

R^{10} and R^{11} are each independently hydrogen, methyl, ethyl, or $-R^8-O-R^5$ (where R^8 is ethylene and R^5 is hydrogen, methyl or ethyl).

8. The compound of Claim 7 which is selected from the group consisting of:

N-(5-chloropyridin-2-yl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(dimethyl)amino-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(3-(*N'*-methyl-*N'*-(2-hydroxyethyl)amino)propoxy)-5-chlorobenzamide; and

N-(5-chloropyridin-2-yl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-amino-5-chlorobenzamide.

9. The compound of Claim 4 wherein

R^1 is chloro;

R^2 is $-N(R^{10})R^{11}$ or $-O-R^8-N(R^{10})R^{11}$ where:

R^8 is methylene, ethylene or propylene; and

R^{10} and R^{11} together with the nitrogen to which they are attached form a *N*-heterocyclic ring containing zero to one additional hetero atoms, where the *N*-heterocyclic ring is optionally substituted by alkyl and is selected from the group consisting of morpholinyl, piperazinyl, pyrrolidinyl or imidazolyl.

10. The compound of Claim 9 selected from the group consisting of:

N-(5-chloropyridin-2-yl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(morpholin-4-yl)-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(4-methylpiperazin-1-yl)-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(3-morpholinylpropoxy)-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(3-(pyrrolidin-1-yl)propoxy)-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(pyrrolidin-1-yl)-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(3-(imidazol-1-yl)propoxy)-5-chlorobenzamide; and

N-(5-chloropyridin-2-yl)-2-[((4-((4-ethylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(morpholin-4-yl)-5-chlorobenzamide.

11. The compound of Claim 2 wherein:

A is =N-;

m is 1 to 3;

n is 1 to 4;

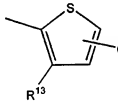
D is -N(R^5)-C(Z)- (where Z is oxygen, sulfur or H_2, and R^5 is hydrogen or alkyl);

E is -C(Z)-N(R^5)- (where Z is oxygen, sulfur or H_2, R^5 is hydrogen or alkyl, and the nitrogen is attached to the pyridinyl ring);

R^1 is halo or haloalkyl;

R^2 is hydrogen, haloalkyl, or -OR^5 where R^5 is hydrogen or alkyl;

R^3 is a radical of the formula (i):



(i)

where r is 1;

R^{13} is halo; and

each R^{14} is independently hydrogen, alkyl, halo, formyl, acetyl, cyano, -R^8-CN, -N(R^{10})R^{11}, -C(R^7)H-N(R^{16})R^{11}, -C(R^7)H-R^8-N(R^{10})R^{11}, -C(R^7)H-N$^{\oplus}$(R^8)(R^{16})$_2$, -C(R^7)H-R^8-N$^{\oplus}$(R^9)(R^{16})$_2$, -C(O)OR^5, -C(R^7)H-C(O)OR^5, -C(R^7)H-R^8-C(O)OR^5, -OR^5, -C(R^7)H-OR^5, -C(R^7)H-R^8-OR^5, -C(R^7)H-O-R^{15}, -S(O)$_p$-R^{15} (where p is 0 to 2), -C(R^7)H-S(O)$_p$-R^{15} (where p is 0 to 2), -C(R^7)H-R^8-S(O)$_p$-R^{15} (where p is 0 to 2), -S(O)$_p$-N(R^5)R^6 (where p is 0 to 2), -C(O)N(R^5)R^6, -C(R^7)H-C(O)N(R^5)R^6, -C(R^7)H-R^8-C(O)N(R^5)R^6, -C(R^7)H-N(R^5)-(R^8-O)$_t$-R^5 (where t is 1 to 6), -C(R^7)H-R^8-N(R^5)-(R^8-O)$_t$-R^5 (where t is 1 to 6), -C(R^7)H-O-(R^8-O)$_t$-R^5 (where t is 1 to 6), -C(R^7)H-R^8-O-(R^8-O)$_t$-R^5 (where t is 1 to 6), -O-R^8-CH(OH)-CH_2-OR^5,

$-C(R^7)H-O-R^8-CH(OH)-CH_2-OR^5$, $-C(R^7)H-N(R^5)-R^8-[CH(OH)]_t-CH_2-OR^5$ (where t is 1 to 6), $-C(R^7)H-N(R^5)-S(O)_z-N(R^{10})R^{11}$, $-C(R^7)H-N(R^{10})-C(NR^{17})-N(R^{10})R^{11}$, $-C(R^7)H-N(R^{10})-C(NR^{17})-R^{10}$, $-C(NR^{17})-N(R^5)R^6$, $-C(R^7)H-C(NR^{17})-N(R^5)R^6$, $-C(R^7)H-O-N(R^5)R^6$, heterocyclyl (wherein the heterocyclyl radical is not attached to the radical of formula (i) through a nitrogen atom and is optionally substituted by alkyl, aryl, aralkyl, halo, haloalkyl, oxo, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ or $-C(O)N(R^5)R^6$), or heterocyclylalkyl (wherein the heterocyclyl radical is not attached to the alkyl radical through a nitrogen atom and is optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, oxo, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ and $-C(O)N(R^5)R^5$); where R^5 and R^6 are each independently hydrogen, alkyl, aryl or aralkyl;

each R^7 is independently hydrogen or alkyl;

each R^8 is independently a straight or branched alkylene, alkylidene or alkylidyne chain;

each R^9 is independently alkyl, aryl or aralkyl;

R^{10} and R^{11} are each independently hydrogen, alkyl, haloalkyl, aryl, aralkyl, formyl, cyano, $-R^8-CN$, $-OR^5$, $-R^8-OR^5$, $-S(O)_p-R^{15}$ (where p is 0 to 2), $-R^8-S(O)_p-R^{15}$ (where p is 0 to 2), $-N(R^5)R^6$, $-R^8-N(R^5)R^6$, $-R^8-C(O)OR^5$, $-C(O)-R^{15}$, $-C(O)NH_2$, $-R^8-C(O)NH_2$, $-C(S)NH_2$, $-C(O)-S-R^5$, $-C(O)-N(R^5)R^{15}$, $-R^8-C(O)-N(R^5)R^{15}$, $-C(S)-N(R^5)R^{15}$, $-R^8-N(R^5)-C(O)H$, $-R^8-N(R^5)-C(O)R^{15}$, $-C(O)O-R^8-N(R^5)R^6$, $-C(N(R^5)R^5)=C(R^{18})R^{10}$, $-R^8-N(R^5)-P(O)(OR^5)_2$, cycloalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, halo and $-OR^5$), heterocyclyl (optionally substituted by alkyl, aryl, aralkyl, halo, haloalkyl, oxo, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-S(O)_p-R^9$ (where p is 0 to 2), $-R^8-S(O)_p-R^9$ (where p is 0 to 2), $-N(R^5)R^6$ or $-C(O)N(R^5)R^6$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, oxo, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-S(O)_p-R^9$ (where p is 0 to 2), $-R^8-S(O)_p-R^9$ (where p is 0 to 2), $-N(R^5)R^6$ and $-C(O)N(R^5)R^6$), where

R^5 and R^6 are each independently hydrogen, alkyl, aryl or aralkyl;

each R^8 is independently a straight or branched alkylene, alkylidene or alkylidyne chain;

each R^9 is independently alkyl, aryl or aralkyl;

each R^{15} is independently alkyl, cycloalkyl, haloalkyl, aryl, aralkyl,

$-R^8$-O-C(O)-R^5, $-R^8$-OR^5, -N(R^5)R^6, $-R^8$-N(R^5)R^6, $-R^8$-C(O)OR^5, heterocyclyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-R^8$-OR^5, -C(O)OR^5, -N(R^5)R^6, and -C(O)N(R^5)R^6), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-R^8$-OR^5, -C(O)OR^5, -N(R^5)R^8, and -C(O)N(R^5)R^6), where

R^5 and R^6 are independently each hydrogen, alkyl, aryl or aralkyl, and

each R^8 is independently a straight or branched alkylene, alkylidene or alkylidyne chain;

or R^5 and R^{15} together with the nitrogen to which they are attached form a *N*-heterocyclic ring containing zero to three additional hetero atoms, where the *N*-heterocyclic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, amino, monoalkylamino, dialkylamino, $-OR^5$, -C(O)OR^5, aminocarbonyl, monoalkylaminocarbonyl, and dialkylaminocarbonyl, where

each R^5 is hydrogen, alkyl, aryl or aralkyl; and

R^{18} is hydrogen, alkyl, aryl, aralkyl, cyano, -C(O)OR^5, or $-NO_2$;

or R^{10} and R^{11} together with the nitrogen to which they are attached form a *N*-heterocyclic ring containing zero to three additional hetero atoms, where the *N*-heterocylic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, halo, haloalkyl, aryl, aralkyl, oxo, nitro, cyano, $-R^8$-CN, =N(R^{17}), $-OR^5$, -C(O)OR^5, $-R^9$-C(O)OR^5, -N(R^5)R^6, $-R^8$-N(R^5)R^6, -C(O)N(R^5)R^6, $-R^8$-C(O)N(R^5)R^6, -N(R^5)-N(R^5)R^6, -C(O)R^5, -C(O)-(R^8-O)$_t$-R^5 (where t is 1 to 6), -S(O)$_p$-R^9 (where p is 0 to 2), $-R^8$-S(O)$_p$-R^9 (where p is 0 to 2), -(R^8-O)$_t$-R^5 (where t is 1 to 6), and heterocyclyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, -C(O)OR^5, -N(R^5)R^6, and -C(O)N(R^5)R^6), where

R^5 and R^6 are each independently hydrogen, alkyl, aryl or aralkyl;

each R^8 is independently a straight or branched alkylene, alkylidene or alkylidyne chain;

each R^9 is independently alkyl, aryl or aralkyl;

each R^{17} is independently hydrogen, alkyl, aryl, aralkyl, cyano, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-R^8-C(O)OR^5$, $-C(O)-N(R^5)R^6$, or $-R^8-C(O)-N(R^5)R^6$, where

R^5 and R^6 are independently each hydrogen, alkyl, aryl or aralkyl, and

each R^8 is independently a straight or branched alkylene, alkylidene or alkylidyne chain;

each R^{16} is independently alkyl, aryl, aralkyl, $-R^8-OR^5$, $-R^8-N(R^5)R^6$, cycloalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, halo and $-OR^5$), heterocyclyl (optionally substituted by alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^8$ or $-C(O)N(R^5)R^6$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^8$ and $-C(O)N(R^5)R^6$), where

R^5 and R^6 are independently each hydrogen, alkyl, aryl or aralkyl, and

each R^8 is independently a straight or branched alkylene, alkylidene or alkylidyne chain; or

both R^{16}s together with the nitrogen to which they are attached (and wherein the R^9 substituent is not present) form an aromatic *N*-heterocyclic ring containing zero to three additional hetero atoms, where the *N*-heterocylic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, $-OR^5$, $-C(O)OR^5$, $-R^8-C(O)OR^5$, $-N(R^5)R^6$, $-R^8-N(R^5)R^6$, $-C(O)R^5$, $-C(O)-(R^8-O)_t-R^5$ (where t is 1 to 6), and $-(R^8-O)_t-R^5$ (where t is 1 to 6), where

R^5 and R^6 are independently each hydrogen, alkyl, aryl or aralkyl, and

each R^8 is independently a straight or branched alkylene, alkylidene or alkylidyne chain;

each R^{17} is independently hydrogen, alkyl, aryl, aralkyl, cyano, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-R^8-C(O)OR^5$, $-C(O)-N(R^5)R^6$, or $-R^8-C(O)-N(R^5)R^6$, where

R^5 and R^6 are independently each hydrogen, alkyl, aryl or aralkyl,

and

each R^8 is independently a straight or branched alkylene, alkylidene or alkylidyne chain;

and R^4 is hydrogen or halo.

12. The compound of Claim 11 wherein:

m is 1;

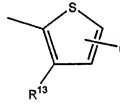
n is 1;

D is -N(H)-C(O)-;

E is -C(O)-N(H)- (where the nitrogen is bonded to the 2-position of the pyridinyl ring);

R^2 is hydrogen, haloalkyl, or $-OR^5$ where R^5 is hydrogen or alkyl;

R^3 is a radical of the formula (i):



(i)

where r is 1;

R^{13} is halo; and

R^{14} is $-C(R^7)H-N(R^{10})R^{11}$ where:

R^7 is hydrogen;

R^{10} and R^{11} are each independently hydrogen, alkyl, haloalkyl, aryl, aralkyl, formyl, cyano, $-R^8-CN$, $-OR^5$, $-R^8-OR^5$, $-S(O)_p-R^{15}$ (where p is 0 to 2), $-R^8-S(O)_p-R^{15}$ (where p is 0 to 2), $-N(R^5)R^6$, $-R^8-N(R^5)R^6$, $-R^8-C(O)OR^5$, $-C(O)-R^{15}$, $-C(O)NH_2$, $-R^8-C(O)NH_2$, $-C(S)NH_2$, $-C(O)-S-R^5$, $-C(O)-N(R^5)R^{15}$, $-R^8-C(O)-N(R^5)R^{15}$, $-C(S)-N(R^5)R^{15}$, $-R^8-N(R^5)-C(O)H$, $-R^8-N(R^5)-C(O)R^{15}$, $-C(O)O-R^8-N(R^5)R^8$, $-C(N(R^5)R^6)=C(R^{18})R^{10}$, $-R^8-N(R^5)-P(O)(OR^5)_2$, cycloalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, halo and $-OR^5$), heterocyclyl (optionally substituted by alkyl, aryl, aralkyl, halo, haloalkyl, oxo, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-S(O)_p-R^9$ (where p is 0 to 2), $-R^8-S(O)_p-R^9$ (where p is 0 to 2), $-N(R^5)R^6$ or $-C(O)N(R^5)R^6$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, oxo, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-S(O)_p-R^9$ (where p

is 0 to 2), $-R^8-S(O)_p-R^9$ (where p is 0 to 2), $-N(R^5)R^6$ and $-C(O)N(R^5)R^6$), where

R^5 and R^6 are each independently hydrogen, alkyl, aryl or aralkyl;

each R^8 is independently a straight or branched alkylene, alkylidene or alkylidyne chain;

each R^9 is independently alkyl, aryl or aralkyl;

each R^{15} is independently alkyl, cycloalkyl, haloalkyl, aryl, aralkyl, $-R^8-O-C(O)-R^5$, $-R^8-OR^5$, $-N(R^5)R^6$, $-R^8-N(R^5)R^6$, $-R^8-C(O)OR^5$, heterocyclyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$, and $-C(O)N(R^5)R^6$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-N(R^5)R^8$, and $-C(O)N(R^5)R^6$), where

R^5 and R^6 are independently each hydrogen, alkyl, aryl or aralkyl, and

each R^8 is independently a straight or branched alkylene, alkylidene or alkylidyne chain;

or R^5 and R^{15} together with the nitrogen to which they are attached form a *N*-heterocyclic ring containing zero to three additional hetero atoms, where the *N*-heterocyclic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, amino, monoalkylamino, dialkylamino, $-OR^5$, $-C(O)OR^5$, aminocarbonyl, monoalkylaminocarbonyl, and dialkylaminocarbonyl, where

each R^5 is hydrogen, alkyl, aryl or aralkyl; and

R^{18} is hydrogen, alkyl, aryl, aralkyl, cyano, $-C(O)OR^5$, or $-NO_2$;

or R^{10} and R^{11} together with the nitrogen to which they are attached form a *N*-heterocyclic ring containing zero to three additional hetero atoms, where the *N*-heterocylic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, halo, haloalkyl, aryl, aralkyl, oxo, nitro, cyano, $-R^8-CN$, $=N(R^{17})$, $-OR^5$, $-C(O)OR^5$, $-R^8-C(O)OR^5$,

$-N(R^5)R^6$, $-R^8-N(R^5)R^6$, $-C(O)N(R^5)R^6$, $-R^8-C(O)N(R^5)R^6$, $-N(R^5)-N(R^5)R^6$, $-C(O)R^5$, $-C(O)-(R^8-O)_t-R^5$ (where t is 1 to 6), $-S(O)_p-R^9$ (where p is 0 to 2), $-R^8-S(O)_p-R^9$ (where p is 0 to 2), $-(R^8-O)_t-R^5$ (where t is 1 to 6), and heterocyclyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$, and $-C(O)N(R^5)R^6$), where

R^5 and R^6 are each independently hydrogen, alkyl, aryl or aralkyl;

each R^8 is independently a straight or branched alkylene, alkylidene or alkylidyne chain;

each R^9 is independently alkyl, aryl or aralkyl;

each R^{17} is independently hydrogen, alkyl, aryl, aralkyl, cyano, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-R^8-C(O)OR^5$, $-C(O)-N(R^5)R^6$, or $-R^8-C(O)-N(R^5)R^6$ where

R^5 and R^6 are independently each hydrogen, alkyl, aryl or aralkyl, and

each R^8 is independently a straight or branched alkylene, alkylidene or alkylidyne chain;

and R^4 is in the 5-position.

13. The compound of Claim 12 wherein:

R^{10} and R^{11} are each independently hydrogen, alkyl, haloalkyl, aryl, aralkyl, formyl, cyano, $-R^8-CN$, $-OR^5$, $-R^8-OR^5$, $-S(O)_p-R^{15}$ (where p is 0 to 2), $-R^8-S(O)_p-R^{15}$ (where p is 0 to 2), $-N(R^5)R^6$, $-R^8-N(R^5)R^6$, $-R^8-C(O)OR^5$, $-C(O)-R^{15}$, $-C(O)NH_2$, $-R^8-C(O)NH_2$, $-C(S)NH_2$, $-C(O)-S-R^5$, $-C(O)-N(R^5)R^{15}$, $-R^8-C(O)-N(R^5)R^{15}$, $-C(S)-N(R^5)R^{15}$, $-R^8-N(R^5)-C(O)H$, $-R^8-N(R^5)-C(O)R^{15}$, $-C(O)O-R^8-N(R^5)R^8$, $-C(N(R^5)R^5)=C(R^{18})R^{10}$, $-R^8-N(R^5)-P(O)(OR^5)_2$, cycloalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, halo and $-OR^5$), heterocyclyl (optionally substituted by alkyl, aryl, aralkyl, halo, haloalkyl, oxo, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-S(O)_p-R^9$ (where p is 0 to 2), $-R^8-S(O)_p-R^9$ (where p is 0 to 2), $-N(R^5)R^6$ or $-C(O)N(R^5)R^5$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, oxo, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-S(O)_p-R^9$ (where p is 0 to 2), $-R^8-S(O)_p-R^9$ (where p is 0 to 2), $-N(R^5)R^6$ and $-C(O)N(R^5)R^6$), where

R^5 and R^6 are each independently hydrogen, alkyl, aryl or aralkyl;

each R^8 is independently a straight or branched alkylene, alkylidene or alkylidyne chain;

each R^9 is independently alkyl, aryl or aralkyl;

each R^{15} is independently alkyl, cycloalkyl, haloalkyl, aryl, aralkyl, $-R^8-O-C(O)-R^5$, $-R^8-OR^5$, $-N(R^5)R^6$, $-R^8-N(R^5)R^6$, $-R^8-C(O)OR^5$, heterocyclyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$, and $-C(O)N(R^5)R^6$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$, and $-C(O)N(R^5)R^6$) where

R^5 and R^6 are independently each hydrogen, alkyl, aryl or aralkyl, and

each R^8 is independently a straight or branched alkylene, alkylidene or alkylidyne chain;

or R^5 and R^{15} together with the nitrogen to which they are attached form a *N*-heterocyclic ring containing zero to three additional hetero atoms, where the *N*-heterocyclic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, amino, monoalkylamino, dialkylamino, $-OR^5$, $-C(O)OR^5$, aminocarbonyl, monoalkylaminocarbonyl, and dialkylaminocarbonyl, where

each R^5 is independently hydrogen, alkyl, aryl or aralkyl; and

R^{18} is hydrogen, alkyl, aryl, aralkyl, cyano, $-C(O)OR^5$, or $-NO_2$.

14. The compound of Claim 13 wherein:

R^{10} is hydrogen, alkyl, or $-R^8-OR^5$; and

R^{11} is hydrogen, alkyl or $-R^8-OR^5$;

where each R^8 is independently a straight or branched alkylene chain, and each R^5 is hydrogen or alkyl.

15. The compound of Claim 14 selected from the group consisting of:

N-(5-chloropyridin-2-yl)-2-[((4-(chloromethyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(2-hydroxyethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(2-hydroxyethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-hydroxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*',*N*'-di(2-hydroxypropyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(3-hydroxypropyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(2-hydroxypropyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-ethyl-*N*'-(2-hydroxyethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(2,2-dimethyl-2-hydroxyethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(2-hydroxyethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-ethoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-(((2-hydroxyethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((methylamino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-(amino)methyl-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((dimethylamino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-ethyl-*N*'-methylamino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-(1-methylethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-(ethylamino)methyl-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide; and

N-(5-chloropyridin-2-yl)-2-[((4-(diethylamino)methyl-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide.

16. The compound of Claim 13 wherein:

R^{10} is hydrogen, alkyl, or $-R^8-N(R^5)R^6$, and

R^{11} is $-S(O)_p-R^{15}$ (where p is 0 to 2) or $-R^8-N(R^5)R^6$ where:

R^5 and R^6 are independently hydrogen or alkyl;

each R^8 is independently a straight or branched alkylene, alkylidene or alkylidyne chain; and

R^{15} is independently alkyl, cycloalkyl, haloalkyl, aryl, aralkyl, $-R^8$-O-C(O)-R^5, $-R^8$-OR^5, $-N(R^5)R^6$, $-R^8$-$N(R^5)R^6$, $-R^8$-C(O)OR^5, heterocyclyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-R^8$-OR^5, -C(O)OR^5, $-N(R^5)R^6$, and -C(O)$N(R^5)R^6$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-R^8$-OR^5, -C(O)OR^5, $-N(R^5)R^6$, and -C(O)$N(R^5)R^6$) where

R^5 and R^6 are independently each hydrogen, alkyl, aryl or aralkyl, and each R^8 is independently a straight or branched alkylene, alkylidene or alkylidyne chain.

17. The compound of Claim 16 selected from the group consisting of:

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(3-(dimethylamino)propyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(methylsulfonyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(2-(dimethylamino)ethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-hydroxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-(methyl)sulfonyl-*N*'-(2-(dimethylamino)ethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(2-(dimethylamino)ethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-((3,5-dimethylisoxazol-4-yl)sulfonyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(methylsulfonyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-hydroxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-((2-(4-hydroxypiperidin-1-yl)ethyl)sulfonyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-((2-(pyrrolidin-1-yl)ethyl)sulfonyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-((dimethylamino)sulfonyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-(2-aminoethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide; and

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-ethyl-*N'*-(4-(dimethylamino)but-3-yn-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide.

18. The compound of Claim 13 wherein:

R^{10} is hydrogen, alkyl or -R^8-OR^5; and

R^{11} is formyl, cyano, -C(O)-R^{15}, -C(O)NH_2, -C(S)NH_2, -C(O)-S-R^5, -C(O)-N(R^5)R^{15}, -C(S)-N(R^5)R^{15}, -R^8-N(R^5)-P(O)(OR^6)$_2$, or -C(N(R^5)R^6)=C(R^{18})R^{10}, where:

each R^5 is hydrogen or alkyl;

R^8 is a straight or branched alkylene chain;

each R^{15} is independently alkyl, cycloalkyl, haloalkyl, aryl, aralkyl, -R^8-O-C(O)-R^5, -R^8-OR^5, -N(R^5)R^6, -R^8-N(R^5)R^6, -R^8-C(O)OR^5, heterocyclyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, -OR^5, -R^8-OR^5, -C(O)OR^5, -N(R^5)R^6, and -C(O)N(R^5)R^6), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, -OR^5, -R^8-OR^5, -C(O)OR^5, -N(R^5)R^6, and -C(O)N(R^5)R^6) where

R^5 and R^6 are independently each hydrogen, alkyl, aryl or aralkyl, and

each R^8 is independently a straight or branched alkylene, alkylidene or alkylidyne chain; and

R^{18} is hydrogen, alkyl, aryl, aralkyl, cyano, -C(O)OR^5, or -NO_2.

19. The compound of Claim 18 selected from the group consisting of:

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N''*-ethylureido)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N''*-(2-carboxyethyl)ureido)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-((4-(2-hydroxyethyl)piperazin-1-yl)carbonyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N''*-(2-morpholin-4-yl)ethyl)thioureido)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-(((4-hydroxypiperidin-1-yl)methyl)carbonyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N''*-(2-hydroxyethyl)ureido)methyl)-3-chlorothiophen-

2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-(*N'*-methylureido)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide; and

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-(2-hydroxyethyl)ureido)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N''*-(2-(chloro)ethyl)ureido)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N''*-(2-(acetoxy)ethyl)ureido)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N''*-(2-(pyrrolidin-1-yl)ethyl)ureido)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N''*-(2-(chloro)ethyl)ureido)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N''*-(2-(((2-hydroxyphenyl)carbonyl)oxy)ethyl)ureido)-methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-cyanoamino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-(2-((fluoromethylcarbonyl)amino)ethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-((2-aminoethoxy)carbonyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-((methylthio)carbonyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-ethyl-*N'*-((phenylthio)carbonyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-(2-nitro-1-(methylamino)ethenyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-(((2-dimethylphosphoramidoethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide.

20. The compound of Claim 13 wherein:

R^{10} is hydrogen, alkyl, haloalkyl, or $-R^8-OR^5$;

R^{11} is cycloalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, halo and $-OR^5$), heterocyclyl (optionally substituted by alkyl, aryl, aralkyl, halo, haloalkyl, oxo, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-S(O)_p-R^9$ (where p is 0 to 2),

$-R^8-S(O)_p-R^9$ (where p is 0 to 2), $-N(R^5)R^6$ or $-C(O)N(R^5)R^6$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, oxo, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-S(O)_p-R^9$ (where p is 0 to 2), $-R^8-S(O)_p-R^9$ (where p is 0 to 2), $-N(R^5)R^6$ and $-C(O)N(R^5)R^6$), where

R^5 and R^6 are each independently hydrogen, alkyl, aryl or aralkyl;

each R^8 is independently a straight or branched alkylene, alkylidene or alkylidyne chain;

each R^9 is independently alkyl, aryl or aralkyl;

each R^{15} is independently alkyl, cycloalkyl, haloalkyl, aryl, aralkyl, $-R^8-O-C(O)-R^5$, $-R^8-OR^5$, $-N(R^5)R^6$, $-R^8-N(R^5)R^6$, $-R^8-C(O)OR^5$, heterocyclyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$, and $-C(O)N(R^5)R^6$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$, and $-C(O)N(R^5)R^6$) where

R^5 and R^6 are independently each hydrogen, alkyl, aryl or aralkyl, and

each R^8 is independently a straight or branched alkylene, alkylidene or alkylidyne chain.

21. The compound of Claim 20 selected from the group consisting of:

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-(2-(morpholin-4-yl)ethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(2-(pyrrolidin-1-yl)ethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(1-methylpiperidin-4-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-hydroxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(4-hydroxycyclohexyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(pyridin-2-yl)methyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-oxazolin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(thiazolin-2-yl)amino)methyl)-3-chlorothiophen-2-

yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-ethyl-*N*'-(oxazolin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-ethyl-*N*'-(thiazolin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(4-(oxo)oxazolin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(pyridin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(dihydro-4(*H*)-1,3-oxazin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(oxazolin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(oxazolin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-hydroxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-(*t*-butyl)-*N*'-(oxazolin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-(((thiazol-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-(2-methoxyethyl)-*N*'-(oxazolin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(oxazol-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(4-trifluoromethyl-5-(methoxycarbonyl)pyrimidin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-ethyl-*N*'-(dihydro-4(*H*)-1,3-oxazin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(5-methyloxazolin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(tetrazol-5-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-ethyl-*N*'-(tetrazol-5-yl)amino)methyl-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-ethyl-*N*'-(4-methyloxazolin-2-yl)amino)methyl-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-(pyrazol-3-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-(2,2,2-trifluoroethyl)-*N'*-(oxazolin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-(4-(ethoxycarbonyl)oxazolin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-(3,4-dihydro-2*H*-pyrrol-5-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-(1,2,4-triazol-4-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-(3,4-dihydro-2*H*-pyrrol-5-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-(pyridin-4-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-(2-amino-6-methylpyrimidin-4-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-((1,2,4-oxadiazol-3-yl)methyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-(2-(imidazol-4-yl)ethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-(3,4,5,6-tetrahydropyridin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-(2-chloropyrimidin-4-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-ethyl-*N'*-(imidazol-2-yl)methyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-(4-aminopyrimidin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-(4-aminopyrimidin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-(4-(methylamino)pyrimidin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-((3-(methoxymethyl)-1,2,4-oxadiazol-5-yl)methyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-((3-((methylthio)methyl)-1,2,4-oxadiazol-5-yl)methyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide; and

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(1,3,2-dioxaphospholan-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide.

22. The compound of Claim 12 wherein:

R^{10} and R^{11} together with the nitrogen to which they are attached form a *N*-heterocyclic ring containing zero to three additional hetero atoms, where the *N*-heterocylic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, halo, haloalkyl, aryl, aralkyl, oxo, nitro, cyano, $-R^8-CN$, $=N(R^{17})$, $-OR^5$, $-C(O)OR^5$, $-R^8-C(O)OR^5$, $-N(R^5)R^6$, $-R^8-N(R^5)R^6$, $-C(O)N(R^5)R^6$, $-R^8-C(O)N(R^5)R^6$, $-N(R^5)-N(R^5)R^6$, $-C(O)R^5$, $-C(O)-(R^8-O)_t-R^5$ (where t is 1 to 6), $-S(O)_p-R^8$ (where p is 0 to 2), $-R^8-S(O)_p-R^9$ (where p is 0 to 2), $-(R^8-O)_t-R^5$ (where t is 1 to 6), and heterocyclyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$, and $-C(O)N(R^5)R^6$), where

R^5 and R^6 are each independently hydrogen, alkyl, aryl or aralkyl;

each R^8 is independently a straight or branched alkylene, alkylidene or alkylidyne chain;

each R^9 is independently alkyl, aryl or aralkyl;

each R^{17} is independently hydrogen, alkyl, aryl, aralkyl, cyano, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-R^8-C(O)OR^5$, $-C(O)-N(R^5)R^6$, or $-R^8-C(O)-N(R^5)R^6$ where

R^5 and R^6 are independently each hydrogen, alkyl, aryl or aralkyl, and

each R^8 is independently a straight or branched alkylene, alkylidene or alkylidyne chain.

23. The compound of Claim 22 wherein the *N*-heterocylic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, halo, haloalkyl, aryl, aralkyl, and nitro.

24. The compound of Claim 23 selected from the group consisting of:

N-(5-chloropyridin-2-yl)-2-[((4-((4,5-dihydropyrazolin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((imidazol-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-

methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((morpholin-4-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((pyrazol-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((hydantoin-3-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((1,4,5,6-tetrahydropyrimidin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((imidazolin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((pyrrolidin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((2,3,4,5,6,7-hexahydro-3,7-dimethyl-2,6-dioxo-1*H*-purin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-hydroxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(pyridin-2-yl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(5-bromopyridin-2-yl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((4-ethylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((2-methylimidazol-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((4-methylimidazol-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((5-methylimidazol-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((2-methylimidazolin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((2,4-dimethylimidazol-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((2,5-dimethylimidazol-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((2-methyl-4-nitroimidazol-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((4,5-dichloroimidazol-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((2-(chloromethyl)imidazolin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide; and

N-(5-chloropyridin-2-yl)-2-[((4-((2-(fluoromethyl)imidazolin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide.

25. The compound of Claim 22 wherein the *N*-heterocylic ring is substituted by one or more substituents selected from the group consisting of alkyl, nitro, $-R^5$-CN, $-OR^5$, $-N(R^5)-N(R^5)R^6$, $-C(O)R^5$, $-S(O)_pR^9$ (where p is 0 to 2), $-(R^8-O)_t-R^5$ (where t is 1 to 6), and heterocyclyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$, and $-C(O)N(R^5)R^6$), where

R^5 and R^6 are each independently hydrogen, alkyl, aryl or aralkyl;

each R^8 is independently a straight or branched alkylene, alkylidene or alkylidyne chain;

each R^9 is independently alkyl, aryl or aralkyl.

26. The compound of Claim 25 selected from the group consisting of:

N-(5-chloropyridin-2-yl)-2-[((4-((4-(hydroxymethyl)imidazol-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((5-(hydroxymethyl)imidazol-1-yl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((2-(methoxymethyl)imidazolin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((2-(hydroxymethyl)imidazol-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((4-formylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((2-(*N'*-amino-*N'*-methylamino)imidazolin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;
N-(5-chloropyridin-2-yl)-2-[((4-((4-hydroxypiperidin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;
N-(5-chloropyridin-2-yl)-2-[((4-((2-(methylthio)imidazolin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;
N-(5-chloropyridin-2-yl)-2-[((4-((4-(methylsulfonyl)piperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;
N-(5-chloropyridin-2-yl)-2-[((4-((2-methyl-4-nitroimidazol-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;
N-(5-chloropyridin-2-yl)-2-[((4-((2-(cyanomethyl)imidazolin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide; and
N-(5-chloropyridin-2-yl)-2-[((4-((4-(pyrimidin-2-yl)piperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide.

27. The compound of Claim 22 wherein the *N*-heterocylic ring is substituted by one or more substituents selected from the group consisting of alkyl, oxo, =N(R^{17}), -C(O)OR^5, -N(R^5)R^6, -C(O)N(R^5)R^6, -(R^8-O)$_r$-R^5, and heterocyclyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, -OR^5, -C(O)OR^5, -N(R^5)R^6, and -C(O)N(R^5)R^6), where

R^5 and R^6 are each independently hydrogen, alkyl, aryl or aralkyl;
each R^8 is independently a straight or branched alkylene, alkylidene or alkylidyne chain;
each R^{17} is independently hydrogen, alkyl, aryl, aralkyl, cyano, -OR^5, -R^8-OR^5, or -C(O)OR^5, -R^8-C(O)OR^5, -C(O)-N(R^5)R^6, -R^8-C(O)-N(R^5)R^6 where
R^5 and R^6 are independently each hydrogen, alkyl, aryl or aralkyl, and
each R^8 is independently a straight or branched alkylene, alkylidene or alkylidyne chain.

28. The compound of Claim 27 wherein the *N*-heterocylic ring is substituted by =N(R^{17}) and is optionally substituted by one or more substituents selected from the group consisting of alkyl, oxo, -C(O)OR^5, -N(R^5)R^6, -C(O)N(R^5)R^6, and -(R^8-O)$_r$-R^5, where

R^5 and R^6 are each independently hydrogen, alkyl, aryl or aralkyl;
each R^8 is independently a straight or branched alkylene, alkylidene or alkylidyne chain;
each R^{17} is independently hydrogen, alkyl, aryl, aralkyl, cyano, -OR^5, -R^8-OR^5, -C(O)OR^5, -R^8-C(O)OR^5, -C(O)-N(R^5)R^6, or -R^8-C(O)-N(R^5)R^6 where

R^5 and R^6 are independently each hydrogen, alkyl, aryl or aralkyl, and each R^8 is independently a straight or branched alkylene, alkylidene or alkylidyne chain.

29. The compound of Claim 28 selected from the group consisting of:

N-(5-chloropyridin-2-yl)-2-[((4-((2-imino-5-methyltetrahydrooxazol-3-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((2-imino-5,5-(dimethyl)tetrahydrooxazol-3-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((2-ethylimino-5,5-(dimethyl)tetrahydrooxazol-3-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((2-imino-5(*S*)-methyltetrahydrooxazol-3-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((2-imino-5(*R*)-methyltetrahydrooxazol-3-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((2-iminotetrahydrooxazol-3-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((2-imino-5-(methoxymethyl)tetrahydrooxazol-3-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((2-imino-4-methyltetrahydrooxazol-3-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*trans*-4,5-dimethyl-2-iminotetrahydrooxazol-3-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*cis*-4,5-dimethyl-2-iminotetrahydrooxazol-3-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((3-methyl-2-imino-2,3-dihydroimidazol-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((2-imino-tetrahydroimidazol-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((2-imino-1,2-dihydropyrimidin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((2-imino-4-(hydroxymethyl)tetrahydrooxazol-3-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((2-iminotetrahydrothiazol-3-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((2-imino-4-oxoimidazolin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((tetrahydro-2-imino-2*H*-pyrimidin-1-ylpyrimidin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((2-(methoxycarbonylamino)imidazolin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((2-(cyanoimino)tetrahydroimidazol-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((2-imino-3-((phenylamino)carbonyl)tetrahydroimidazol-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*cis*-4,5-dimethoxy-2-iminotetrahydroimidazol-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((2-amino-4-imino-1,4-dihydropyrimidin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((2-((2-hydroxyethyl)imino)tetrahydroimidazol-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((2-iminopiperidin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((4-imino-1(4*H*)-pyridinyl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((2-imino-1(2*H*)-pyridin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((2-(ethylimino)pyrrolidin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide; and

N-(5-chloropyridin-2-yl)-2-[((4-((2-(((aminocarbonyl)methyl)imino)tetrahydroimidazol-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide.

30. The compound of Claim 22 wherein the *N*-heterocylic ring is substituted by $-N(R^5)R^6$ and optionally substituted by one or more substituents selected from the group consisting of alkyl, oxo, $-N(R^5)R^6$, $-OR^5$, and $-C(O)N(R^5)R^6$, where R^5 and R^6 are each independently hydrogen, alkyl, aryl or aralkyl.

31. The compound of Claim 30 selected from the group consisting of:

N-(5-chloropyridin-2-yl)-2-[((4-((2-aminoimidazol-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((5-aminotetrazol-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((3-amino-1,2,4-triazol-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((3,5-diamino-4*H*-1,2,4-triazol-4-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((4-amino-5-(aminocarbonyl)imidazol-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((2,6-diaminopurin-9-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((2,6-diaminopurin-7-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((5-amino-2-oxo-2*H*-pyrimidin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((6-aminopurin-9-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((6-aminopurin-7-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((2-amino-6-oxopurin-9-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((2-amino-6-oxopurin-7-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((5-(dimethylamino)-1,2,4-oxadiazol-3-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((5-amino-1,2,4-oxadiazol-3-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((2-(methylamino)imidazol-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((2,4-diamino-6-hydroxypyrimidin-5-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((2-(ethylamino)imidazol-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((2-(1-methylethyl)imidazol-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((3-dimethylamino-5-methylpyrazol-1-yl)methyl)-3-

chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide; and
N-(5-chloropyridin-2-yl)-2-[((4-((3-dimethylamino-5-methylpyrazol-2-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide.

32. The compound of Claim 11 wherein:

each R^{14} is independently alkyl, $-R^8$-CN, $-C(R^7)H-R^8-N(R^{10})R^{11}$, $-C(R^7)H-R^8-N^{\oplus}(R^5)(R^{16})_2$, $-C(R^7)H-OR^5$, $-C(R^7)H-R^8-OR^5$, $-C(R^7)H-O-R^{15}$, $-C(R^7)H-S(O)_p-R^{15}$ (where p is 0 to 2), $-C(R^7)H-N(R^5)-(R^8-O)_t-R^5$ (where t is 1 to 6), $-C(R^7)H-N(R^5)-R^8-[CH(OH)]_t-CH_2-OR^5$ (where t is 1 to 6), $-C(R^7)H-N(R^5)-S(O)_2-N(R^{10})R^{11}$, $-C(R^7)H-O-N(R^5)R^6$, or heterocyclyl (wherein the heterocyclyl radical is not attached to the radical of formula (i) through a nitrogen atom and is optionally substituted by alkyl, aryl, aralkyl, halo, haloalkyl, oxo, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ or $-C(O)N(R^5)R^5$), where

R^5 and R^6 are each independently hydrogen, alkyl, aryl or aralkyl;

each R^7 is independently hydrogen or alkyl;

each R^8 is independently a straight or branched alkylene, alkylidene or alkylidyne chain;

R^{10} and R^{11} are each independently hydrogen, alkyl, haloalkyl, aryl, aralkyl, formyl, cyano, $-R^8$-CN, $-OR^5$, $-R^8-OR^5$, $-S(O)_p-R^{15}$ (where p is 0 to 2), $-R^8-S(O)_p-R^{15}$ (where p is 0 to 2), $-N(R^5)R^6$, $-R^8-N(R^5)R^6$, $-R^8-C(O)OR^5$, $-C(O)-R^{15}$, $-C(O)NH_2$, $-R^8-C(O)NH_2$, $-C(S)NH_2$, $-C(O)-S-R^5$, $-C(O)-N(R^5)R^{15}$, $-R^8-C(O)-N(R^5)R^{15}$, $-C(S)-N(R^5)R^{15}$, $-R^8-N(R^5)-C(O)H$, $-R^8-N(R^5)-C(O)R^{15}$, $-C(O)O-R^8-N(R^5)R^6$, $-C(N(R^5)R^6)=C(R^{18})R^{10}$, $-R^8-N(R^5)-P(O)(OR^5)_2$, cycloalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, halo and $-OR^5$), heterocyclyl (optionally substituted by alkyl, aryl, aralkyl, halo, haloalkyl, oxo, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-S(O)_p-R^9$ (where p is 0 to 2), $-R^8-S(O)_p-R^9$ (where p is 0 to 2), $-N(R^5)R^6$ or $-C(O)N(R^5)R^6$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, oxo, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-S(O)_p-R^9$ (where p is 0 to 2), $-R^8-S(O)_p-R^9$ (where p is 0 to 2), $-N(R^5)R^6$ and $-C(O)N(R^5)R^6$), where

R^5 and R^6 are each independently hydrogen, alkyl, aryl or aralkyl;

each R^9 is independently a straight or branched alkylene, alkylidene or alkylidyne chain;

each R^9 is independently alkyl, aryl or aralkyl;

each R^{15} is independently alkyl, cycloalkyl, haloalkyl, aryl, aralkyl, $-R^8-O-C(O)-R^5$, $-R^8-OR^5$, $-N(R^5)R^6$, $-R^8-N(R^5)R^6$, $-R^8-C(O)OR^5$, heterocyclyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-N(R^5)R^8$, and $-C(O)N(R^5)R^8$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$, and $-C(O)N(R^5)R^6$), where

R^5 and R^6 are independently each hydrogen, alkyl, aryl or aralkyl, and

each R^8 is independently a straight or branched alkylene, alkylidene or alkylidyne chain;

or R^5 and R^{15} together with the nitrogen to which they are attached form a *N*-heterocyclic ring containing zero to three additional hetero atoms, where the *N*-heterocyclic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, amino, monoalkylamino, dialkylamino, $-OR^5$, $-C(O)OR^5$, aminocarbonyl, monoalkylaminocarbonyl, and dialkylaminocarbonyl, where

each R^5 is hydrogen, alkyl, aryl or aralkyl; and

R^{18} is hydrogen, alkyl, aryl, aralkyl, cyano, $-C(O)OR^5$, or $-NO_2$;

or R^{10} and R^{11} together with the nitrogen to which they are attached form a *N*-heterocyclic ring containing zero to three additional hetero atoms, where the *N*-heterocyclic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, halo, haloalkyl, aryl, aralkyl, oxo, nitro, cyano, $-R^8-CN$, $=N(R^{17})$, $-OR^5$, $-C(O)OR^5$, $-R^8-C(O)OR^5$, $-N(R^5)R^6$, $-R^8-N(R^5)R^6$, $-C(O)N(R^5)R^6$, $-R^8-C(O)N(R^5)R^6$, $-N(R^5)-N(R^5)R^6$, $-C(O)R^5$, $-C(O)-(R^8-O)_t-R^5$ (where t is 1 to 6), $-S(O)_p-R^9$ (where p is 0 to 2), $-R^8-S(O)_p-R^9$ (where p is 0 to 2), $-(R^8-O)_t-R^5$ (where t is 1 to 6), and heterocyclyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$,

$-C(O)OR^5$, $-N(R^5)R^8$, and $-C(O)N(R^5)R^8$), where

R^5 and R^6 are each independently hydrogen, alkyl, aryl or aralkyl;

each R^8 is independently a straight or branched alkylene, alkylidene or alkylidyne chain;

each R^9 is independently alkyl, aryl or aralkyl;

each R^{17} is independently hydrogen, alkyl, aryl, aralkyl, cyano, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-R^8-C(O)OR^5$, $-C(O)-N(R^5)R^8$, or $-R^8-C(O)-N(R^5)R^6$, where

R^5 and R^6 are independently each hydrogen, alkyl, aryl or aralkyl, and

each R^8 is independently a straight or branched alkylene, alkylidene or alkylidyne chain;

each R^{16} is independently alkyl, aryl, aralkyl, $-R^8-OR^5$, $-R^8-N(R^5)R^6$, cycloalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, halo and $-OR^5$), heterocyclyl (optionally substituted by alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ or $-C(O)N(R^5)R^6$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ and $-C(O)N(R^5)R^8$), where

R^5 and R^6 are independently each hydrogen, alkyl, aryl or aralkyl, and

each R^8 is independently a straight or branched alkylene, alkylidene or alkylidyne chain; or

both R^{16}s together with the nitrogen to which they are attached (and wherein the R^9 substituent is not present) form an aromatic *N*-heterocyclic ring containing zero to three additional hetero atoms, where the *N*-heterocylic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-R^8-C(O)OR^5$, $-N(R^5)R^8$, $-R^8-N(R^5)R^6$, $-C(O)R^5$, $-C(O)-(R^8-O)_t-R^5$ (where t is 1 to 6), and $-(R^8-O)_t-R^5$ (where t is 1 to 6), where

R^5 and R^6 are independently each hydrogen, alkyl, aryl or aralkyl, and

each R^8 is independently a straight or branched alkylene, alkylidene or alkylidyne chain.

33. The compound of Claim 32 selected from the group consisting of:

N-(5-chloropyridin-2-yl)-2-[((4-((pyridinium-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-hydroxy-5-chlorobenzamide,

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(2-(hydroxyethoxy)ethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((methylsulfinyl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(2,3-dihydroxypropyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-(((2-hydroxyethyl)sulfinyl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((pyridinium-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-methyl-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-cyanomethyl-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-(2-methylaminoethyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-(hydroxy)methyl-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-(((imidazol-2-yl)thio)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((imidazolin-2-yl)thio)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-(((5-hydroxymethyl-1-methylimidazol-2-yl)thio)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-(((diethylamino)oxy)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide; and

N-(5-chloropyridin-2-yl)-2-[((4-(imidazolin-2-yl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide.

34. The compound of Claim 11 wherein:

each R^{14} is independently $-C(R^7)H-N(R^{10})-C(NR^{17})-N(R^{10})R^{11}$, $-C(R^7)H-N(R^{10})-C(NR^{17})-R^{10}$, or $-C(R^7)H-C(NR^{17})-N(R^5)R^6$, where

R^5 and R^6 are each independently hydrogen, alkyl, aryl or aralkyl;

each R^7 is independently hydrogen or alkyl;

each R^9 is independently alkyl, aryl or aralkyl;

R^{10} and R^{11} are each independently hydrogen, alkyl, haloalkyl, aryl, aralkyl, formyl, cyano, $-R^8-CN$, $-OR^5$, $-R^8-OR^5$, $-S(O)_p-R^{15}$ (where p is 0 to 2), $-R^8-S(O)_p-R^{15}$ (where p is 0 to 2), $-N(R^5)R^6$, $-R^8-N(R^5)R^6$, $-R^8-C(O)OR^5$, $-C(O)-R^{15}$, $-C(O)NH_2$, $-R^8-C(O)NH_2$, $-C(S)NH_2$, $-C(O)-S-R^5$, $-C(O)-N(R^5)R^{15}$, $-R^8-C(O)-N(R^5)R^{15}$, $-C(S)-N(R^5)R^{15}$, $-R^8-N(R^5)-C(O)H$, $-R^8-N(R^5)-C(O)R^{15}$, $-C(O)O-R^8-N(R^5)R^6$, $-C(N(R^5)R^5)=C(R^{15})R^{10}$, $-R^8-N(R^5)-P(O)(OR^5)_2$, cycloalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, halo and $-OR^5$), heterocyclyl (optionally substituted by alkyl, aryl, aralkyl, halo, haloalkyl, oxo, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-S(O)_p-R^9$ (where p is 0 to 2), $-R^8-S(O)_p-R^9$ (where p is 0 to 2), $-N(R^5)R^6$ or $-C(O)N(R^5)R^6$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, oxo, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-S(O)_p-R^9$ (where p is 0 to 2), $-R^8-S(O)_p-R^9$ (where p is 0 to 2), $-N(R^5)R^6$ and $-C(O)N(R^5)R^6$), where

R^5 and R^6 are each independently hydrogen, alkyl, aryl or aralkyl;

each R^8 is independently a straight or branched alkylene, alkylidene or alkylidyne chain;

each R^9 is independently alkyl, aryl or aralkyl;

each R^{15} is independently alkyl, cycloalkyl, haloalkyl, aryl, aralkyl, $-R^8-O-C(O)-R^5$, $-R^8-OR^5$, $-N(R^5)R^5$, $-R^8-N(R^5)R^5$, $-R^8-C(O)OR^5$, heterocyclyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$, and $-C(O)N(R^5)R^6$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$, and $-C(O)N(R^5)R^6$), where

R^5 and R^6 are independently each hydrogen, alkyl, aryl or aralkyl, and

each R^8 is independently a straight or branched

alkylene, alkylidene or alkylidyne chain;

or R^5 and R^{15} together with the nitrogen to which they are attached form a *N*-heterocyclic ring containing zero to three additional hetero atoms, where the *N*-heterocyclic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, amino, monoalkylamino, dialkylamino, $-OR^5$, $-C(O)OR^5$, aminocarbonyl, monoalkylaminocarbonyl, and dialkylaminocarbonyl, where

each R^5 is hydrogen, alkyl, aryl or aralkyl; and

R^{18} is hydrogen, alkyl, aryl, aralkyl, cyano, $-C(O)OR^5$, or $-NO_2$;

or R^{10} and R^{11} together with the nitrogen to which they are attached form a *N*-heterocyclic ring containing zero to three additional hetero atoms, where the *N*-heterocylic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, halo, haloalkyl, aryl, aralkyl, oxo, nitro, cyano, $-R^8$-CN, $=N(R^{17})$, $-OR^5$, $-C(O)OR^5$, $-R^8$-$C(O)OR^5$, $-N(R^5)R^6$, $-R^8$-$N(R^5)R^6$, $-C(O)N(R^5)R^6$, $-R^8$-$C(O)N(R^5)R^6$, $-N(R^5)$-$N(R^5)R^6$, $-C(O)R^5$, $-C(O)$-$(R^8$-$O)_t$-R^5 (where t is 1 to 6), $-S(O)_p$-R^9 (where p is 0 to 2), $-R^8$-$S(O)_p$-R^9 (where p is 0 to 2), $-(R^8$-$O)_t$-R^5 (where t is 1 to 6), and heterocyclyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$, and $-C(O)N(R^5)R^6$), where

R^5 and R^6 are each independently hydrogen, alkyl, aryl or aralkyl;

each R^8 is independently a straight or branched alkylene, alkylidene or alkylidyne chain;

each R^9 is independently alkyl, aryl or aralkyl;

each R^{17} is independently hydrogen, alkyl, aryl, aralkyl, cyano, $-OR^5$, $-R^8$-OR^5, $-C(O)OR^5$, $-R^8$-$C(O)OR^5$, $-C(O)$-$N(R^5)R^6$, or $-R^8$-$C(O)$-$N(R^5)R^6$, where

R^5 and R^6 are independently each hydrogen, alkyl, aryl or aralkyl, and

each R^8 is independently a straight or branched alkylene, alkylidene or alkylidyne chain;

each R^{17} is independently hydrogen, alkyl, aryl, aralkyl, cyano, $-OR^5$, $-R^8$-OR^5, $-C(O)OR^5$, $-R^8$-$C(O)OR^5$, $-C(O)$-$N(R^5)R^6$, or $-R^8$-$C(O)$-$N(R^5)R^6$, where

R^5 and R^6 are independently each hydrogen, alkyl, aryl or aralkyl,
and
each R^8 is independently a straight or branched alkylene,
alkylidene or alkylidyne chain.

35. The compound of Claim 34 selected from the group consisting of:
N-(5-chloropyridin-2-yl)-2-[((4-(((amidino)(methyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;
N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-(1-iminoethyl)-*N*'-methylamino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;
N-(5-chloropyridin-2-yl)-2-[((4-(*N*',*N*''-dimethyl-*N*'''-cyanoguanidino)methyl-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;
N-(5-chloropyridin-2-yl)-2-[((4-(*N*'-methyl-*N*''-hydroxyguanidino)methyl-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;
N-(5-chloropyridin-2-yl)-2-[((4-(*N*'-methyl-*N*''-(2-aminoethyl)-*N*'''-cyanoguanidino)methyl-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;
N-(5-chloropyridin-2-yl)-2-[((4-(*N*'-methyl-*N*''-aminoguanidino)methyl-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;
N-(5-chloropyridin-2-yl)-2-[((4-(*N*',*N*''-dimethyl-*N*'''-(aminocarbonyl)guanidino)methyl-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;
N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-(imino(phenyl)methyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;
N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-(1-imino-2-(aminocarbonyl)ethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;
N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-(1-imino-4,4,4-trifluorobutyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;
N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-(imino(pyridin-4-yl)methyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;
N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-(imino(thiophen-2-yl)methyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;
N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-(imino(pyrazin-2-yl)methyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;
N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-(cyclopropyl(imino)methyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;
N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-ethyl-*N*'-(3-cyano-1-iminopropyl)amino)methyl)-3-

chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(1-imino-4,4,4-trifluorobutyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide; and

N-(5-chloropyridin-2-yl)-2-[((4-(2-amino-2-(hydroxyimino)ethyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide.

36. The compound of Claim 2 wherein:

A is =N-;

m is 1;

n is 1;

D is -N(H)-C(O)-;

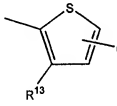
E is -C(O)-N(H)- (where the nitrogen is bonded to the 2-position of the pyridinyl ring);

R^2 is $-N(R^{10})R^{11}$ where:

R^{10} and R^{11} are each independently hydrogen, alkyl or $-R^8-O-R^5$ where R^8 is an alkylene chain, and R^5 is hydrogen or alkyl; or

R^{10} and R^{11} together with the nitrogen to which they are attached form a *N*-heterocyclic ring containing zero to three additional hetero atoms, where the *N*-heterocylic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl and $-C(O)OR^5$ where R^5 is hydrogen or alkyl;

R^3 is a radical of the formula (i):



(i)

where r is 1;

R^{13} is halo; and

R^{14} is $-C(R^7)H-N(R^{10})R^{11}$ or $-C(R^7)H-N(R^5)-R^8-[CH(OH)]_t-CH_2-OR^5$ (where t is 1 to 3)

where:

each R^5 is independently hydrogen or alkyl;

R^7 is hydrogen;

R^8 is a straight or branched alkylene chain;

R^{10} and R^{11} are each independently hydrogen, alkyl, formyl, $-R^8-OR^5$, $-S(O)_p-R^{15}$ (where p is 0 to 2), $-R^8-N(R^5)R^6$, $-R^8-C(O)OR^5$, $-C(O)-R^{15}$, $-C(O)NH_2$,

$-C(S)NH_2$, $-C(O)-N(R^5)R^{15}$, $-C(S)-N(R^5)R^{15}$, cycloalkyl (optionally substituted by $-OR^5$), heterocyclyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, haloalkyl, oxo, $-OR^5$, and $-C(O)OR^5$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, haloalkyl, oxo, $-OR^5$, and $-C(O)OR^5$), where:

each R^5 and R^6 is independently hydrogen or alkyl;

each R^8 is independently a straight or branched alkylene chain; and

each R^{15} is alkyl, $-R^8-OR^5$, $-R^8-C(O)OR^5$, heterocyclyl (optionally substituted by $-R^8-OR^5$), or heterocyclylalkyl (optionally substituted by $-OR^5$);

or R^{10} and R^{11} together with the nitrogen to which they are attached form a *N*-heterocyclic ring containing zero to three additional hetero atoms, where the *N*-heterocylic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, oxo, $=N(R^{17})$, $-OR^5$, $-R^8-OR^5$, and $-N(R^5)R^6$; where

each R^5 and R^6 is independently hydrogen or alkyl;

R^8 is a straight or branched alkylene chain; and

each R^{17} is independently hydrogen, alkyl, aryl, aralkyl, cyano, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-R^8-C(O)OR^5$, $-C(O)-N(R^5)R^6$, or $-R^8-C(O)-N(R^5)R^6$;

and R^4 is in the 5-position and is hydrogen or halo.

37. The compound of Claim 36 wherein:

R^2 is $-N(R^{10})R^{11}$ where:

R^{10} and R^{11} are each independently hydrogen, alkyl or $-R^8-O-R^5$ where R^8 is an alkylene chain, and R^5 is hydrogen or alkyl.

38. The compound of Claim 37 wherein:

R^{14} is $-C(R^7)H-N(R^{10})R^{11}$ where:

R^7 is hydrogen;

R^{10} and R^{11} are each independently hydrogen, alkyl, formyl, $-R^8-OR^5$, $-S(O)_p-R^{15}$ (where p is 0 to 2), $-R^8-N(R^5)R^6$, $-R^8-C(O)OR^5$, $-C(O)-R^{15}$, $-C(O)NH_2$, $-C(S)NH_2$, $-C(O)-N(R^5)R^{15}$, $-C(S)-N(R^5)R^{15}$, cycloalkyl (optionally substituted by $-OR^5$), heterocyclyl (optionally substituted by one or more substituents selected from the

group consisting of alkyl, haloalkyl, oxo, -OR^5, and -$C(O)OR^5$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, haloalkyl, oxo, -OR^5, and -$C(O)OR^5$); where:

each R^5 and R^6 is hydrogen or alkyl;

each R^8 is independently a straight or branched alkylene chain; and

each R^{15} is alkyl, -R^8-OR^5, -R^8-$C(O)OR^5$, heterocyclyl (optionally substituted by -R^8-OR^5), or heterocyclylalkyl (optionally substituted by -OR^5);

or R^{10} and R^{11} together with the nitrogen to which they are attached form a *N*-heterocyclic ring containing zero to three additional hetero atoms, where the *N*-heterocyclic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, oxo, =$N(R^{17})$, -OR^5, -R^8-OR^5, and -$N(R^5)R^6$; where:

each R^5 is hydrogen or alkyl;

R^8 is straight or branched alkylene chain; and

each R^{17} is independently hydrogen, alkyl, aryl, aralkyl, cyano, -OR^5, -R^8-OR^5, -$C(O)OR^5$, -R^8-$C(O)OR^5$, -$C(O)$-$N(R^5)R^6$, or -R^8-$C(O)$-$N(R^5)R^6$.

39. The compound of Claim 38 selected from the group consisting of:

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(3-(dimethylamino)propyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(dimethyl)amino-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(2-(dimethylamino)ethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(dimethyl)amino-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(1-methylpiperidin-4-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(dimethyl)amino-5-chlorobenzamide; and

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(2-hydroxyethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(di(2-methoxyethyl)amino)-5-chlorobenzamide.

40. The compound of Claim 36 wherein

R^2 is -$N(R^{10})R^{11}$ where:

R^{10} and R^{11} together with the nitrogen to which they are attached form a *N*-heterocyclic ring containing zero to three additional hetero atoms, where the *N*-heterocyclic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl and -$C(O)OR^5$ where R^5 is hydrogen or alkyl.

41. The compound of Claim 40 selected from the group consisting of:

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-(2-(dimethylamino)ethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(morpholin-4-yl)-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-(2-hydroxyethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(morpholin-4-yl)-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-(2-hydroxyethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(morpholin-4-yl)-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-(1-methylpiperidin-4-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(morpholin-4-yl)-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-(2-(morpholin-4-yl)ethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(morpholin-4-yl)-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-(methylsulfonyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(morpholin-4-yl)-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-(3-(dimethylamino)propyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(morpholin-4-yl)-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-(2-(pyrrolidin-1-yl)ethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(morpholin-4-yl)-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-(2-methoxyethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(morpholin-4-yl)-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methylsulfonyl-*N'*-(2-(pyrrolidin-1-yl)ethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(morpholin-4-yl)-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N''*-methyl-*N'*-(2-(pyrrolidin-1-yl)ethyl)ureido)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(morpholin-4-yl)-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-(methylsulfonyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(4-methylpiperazin-1-yl)-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-(2-hydroxyethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(4-methylpiperazin-1-yl)-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-(2-hydroxyethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(pyrrolidin-1-yl)-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-(1-methylethyl)-*N'*-(2-(pyrrolidin-1-yl)ethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(morpholin-4-yl)-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-(2-hydroxyethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(4-(ethoxycarbonyl)piperidin-1-yl)-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-(2-hydroxyethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(4-(carboxy)piperidin-1-yl)-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-(2,3-dihydroxypropyl)amino)methyl)-3-

chlorothiophen-2-yl)carbonyl)amino]-3-(morpholin-4-yl)-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N''*-ethylureido)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(4-ethylpiperazin-1-yl)-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-(oxazolin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(morpholin-4-yl)-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-ethyl-*N'*-(oxazolin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(morpholin-4-yl)-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-(4-trifluoromethyl-5-(methoxycarbonyl)pyrimidin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(morpholin-4-yl)-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-(4-trifluoromethyl-5-carboxypyrimidin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(morpholin-4-yl)-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((2-iminotetrahydrooxazol-3-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(morpholin-4-yl)-5-chlorobenzamide; and

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-(tetrazol-5-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(morpholin-4-yl)-5-chlorobenzamide.

42. The compound of Claim 2 wherein:

A is =N-;

m is 1;

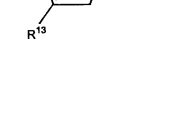
n is 1;

D is -N(H)-C(O)-;

E is -C(O)-N(H)- (where the nitrogen is bonded to the 2-position of the pyridinyl ring);

R^2 is $-O-(R^6-O)_t-R^5$ (where t is 1 to 3) or $-O-(R^6-O)_t-R^{19}$ where R^5 is hydrogen or alkyl, each R^6 is independently a straight or branched alkylene chain, and R^{19} is heterocyclyl (optionally substituted by alkyl, aryl, aralkyl, halo, or haloalkyl);

R^3 is a radical of the formula (i):



(i)

where r is 1;

R^{13} is halo; and

R^{14} is $-C(R^7)H-N(R^{10})R^{11}$ where:

R^7 is hydrogen;

R^{10} and R^{11} are each independently hydrogen, alkyl, formyl, $-R^8-OR^5$, $-S(O)_p-R^{15}$ (where p is 0 to 2), $-R^8-N(R^5)R^6$, $-R^8-C(O)OR^5$, $-C(O)-R^{15}$, $-C(O)NH_2$, $-C(S)NH_2$, $-C(O)-N(R^5)R^{15}$, $-C(S)-N(R^5)R^{15}$, cycloalkyl (optionally substituted by $-OR^5$), heterocyclyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, haloalkyl, oxo, $-OR^5$, and $-C(O)OR^5$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, haloalkyl, oxo, $-OR^5$, and $-C(O)OR^5$); where:

each R^5 and R^6 is hydrogen or alkyl;

each R^8 is independently a straight or branched alkylene chain; and

each R^{15} is alkyl, $-R^8-OR^5$, $-R^8-C(O)OR^5$, heterocyclyl (optionally substituted by $-R^8-OR^5$), or heterocyclylalkyl (optionally substituted by $-OR^5$);

or R^{10} and R^{11} together with the nitrogen to which they are attached form a *N*-heterocyclic ring containing zero to three additional hetero atoms, where the *N*-heterocylic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, oxo, $=N(R^{17})$, $-OR^5$, $-R^8-OR^5$, and $-N(R^5)R^6$; where

each R^5 is hydrogen or alkyl;

R^8 is straight or branched alkylene chain; and

each R^{17} is independently hydrogen, alkyl, aryl, aralkyl, cyano, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-R^8-C(O)OR^5$, $-C(O)-N(R^5)R^6$, or $-R^8-C(O)-N(R^5)R^6$; and

R^4 is in the 5-position and is hydrogen or halo.

43. The compound of Claim 42 selected from the group consisting of:

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(2-(dimethylamino)ethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2-hydroxyethoxy)-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(1-methylpiperidin-4-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2-hydroxyethoxy)-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(2-(pyrrolidin-1-yl)ethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2-methoxyethoxy)-5-chlorobenzamide,

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(2-(pyrrolidin-1-yl)ethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2-hydroxyethoxy)-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(2,3-dihydroxypropyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2-methoxyethoxy)-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-ethyl-*N*'-(2-hydroxyethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2-methoxyethoxy)-5-chlorobenzamide,

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(2-hydroxyethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2-methoxyethoxy)-5-chlorobenzamide,

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(oxazolin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-((2-(2-methoxyethoxy)ethoxy)-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(methylsulfonyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-((2-(2-methoxyethoxy)ethoxy)-5-chlorobenzamide; and

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(2-hydroxyethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(3-(pyridin-3-yloxy)propoxy)-5-chlorobenzamide.

44. The compound of Claim 2 wherein:

A is =N-;

m is 1;

n is 1;

D is -N(H)-C(O)-;

E is -C(O)-N(H)- (where the nitrogen is bonded to the 2-position of the pyridinyl ring);

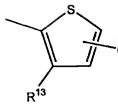
R^2 is $-O-R^8-N(R^{10})R^{11}$ where:

R^8 is a straight or branched alkylene chain; and

R^{10} and R^{11} are each independently hydrogen, alkyl or $-R^8-O-R^5$ where R^8 is an alkylene chain, and R^5 is hydrogen or alkyl; or

R^{10} and R^{11} together with the nitrogen to which they are attached form a *N*-heterocyclic ring containing zero to three additional hetero atoms, where the *N*-heterocylic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl and $-C(O)OR^5$ where R^5 is hydrogen or alkyl;

R^3 is a radical of the formula (i):



(i)

where r is 1;

R^{13} is halo; and

R^{14} is $-C(R^7)H-N(R^{10})R^{11}$ where:

R^7 is hydrogen;

R^{10} and R^{11} are each independently hydrogen, alkyl, formyl, $-R^8-OR^5$, $-S(O)_p-R^{15}$ (where p is 0 to 2), $-R^8-N(R^5)R^6$, $-R^8-C(O)OR^5$, $-C(O)-R^{15}$, $-C(O)NH_2$, $-C(S)NH_2$, $-C(O)-N(R^5)R^{15}$, $-C(S)-N(R^5)R^{15}$, cycloalkyl (optionally substituted by $-OR^5$), heterocyclyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, haloalkyl, oxo, $-OR^5$, and $-C(O)OR^5$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, haloalkyl, oxo, $-OR^5$, and $-C(O)OR^5$), where:

each R^5 and R^6 is hydrogen or alkyl;

each R^8 is independently a straight or branched alkylene chain; and

each R^{15} is alkyl, $-R^8-OR^5$, $-R^8-C(O)OR^5$, heterocyclyl (optionally substituted by $-R^8-OR^5$), or heterocyclylalkyl (optionally substituted by $-OR^5$); and

R^4 is in the 5-position and is hydrogen or halo.

45. The compound of Claim 44 selected from the group consisting of:

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(1-methylpiperidin-4-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(3-(morpholin-4-yl)propoxy)-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(2-hydroxyethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(3-(pyrrolidin-1-yl)propoxy)-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(2-hydroxyethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(3-(morpholin-4-yl)propoxy)-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(2-hydroxyethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2-(imidazol-1-yl)ethoxy)-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N*'-methyl-*N*'-(2-hydroxyethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(3-(imidazol-1-yl)propoxy)-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-(methylsulfonyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2-(pyrrolidin-1-yl)ethoxy)-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-(methylsulfonyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2-(imidazol-1-yl)ethoxy)-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-(2-hydroxyethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2-(pyrrolidin-1-yl)ethoxy)-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-(methylsulfonyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(3-(4-ethylpiperazin-1-yl)propoxy)-5-chlorobenzamide; and

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-(methylsulfonyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2-aminoethoxy)-5-chlorobenzamide.

46. The compound of Claim 2 wherein:

A is =N-;

m is 1;

n is 1;

D is -N(H)-C(O)-;

E is -C(O)-N(H)- (where the nitrogen is bonded to the 2-position of the pyridinyl ring);

R^2 is $-O-R^8-O-C(O)R^5$, $-O-R^8-CH(OH)-CH_2-N(R^{10})R^{11}$, or $-O-R^8-CH(OH)-CH_2-OR^5$ where

each R^5 is hydrogen or alkyl;

R^8 is a straight or branched alkylene chain; and

R^{10} and R^{11} are each independently hydrogen, alkyl or $-R^8-O-R^5$ where R^8 is an alkylene chain, and R^5 is hydrogen or alkyl; or

R^{10} and R^{11} together with the nitrogen to which they are attached form a *N*-heterocyclic ring containing zero to three additional hetero atoms, where the *N*-heterocylic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl and $-C(O)OR^5$ where R^5 is hydrogen or alkyl;

R^3 is a radical of the formula (i):

(i)

where r is 1;

R^{13} is halo; and

R^{14} is $-C(R^7)H-N(R^{10})R^{11}$ or $-C(R^7)H-N(R^5)-S(O)_2-N(R^{10})R^{11}$ where:

R^5 is hydrogen or alkyl;

R^7 is hydrogen;

R^{10} and R^{11} are each independently hydrogen, alkyl, formyl, $-R^8-OR^5$, $-S(O)_p-R^{15}$ (where p is 0 to 2), $-R^8-N(R^5)R^6$, $-R^8-C(O)OR^5$, $-C(O)-R^{15}$, $-C(O)NH_2$, $-C(S)NH_2$, $-C(O)-N(R^5)R^{15}$, $-C(S)-N(R^5)R^{15}$, cycloalkyl (optionally substituted by $-OR^5$), heterocyclyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, haloalkyl, oxo, $-OR^5$, and $-C(O)OR^5$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, haloalkyl, oxo, $-OR^5$, and $-C(O)OR^5$); where:

each R^5 and R^6 is hydrogen or alkyl;

each R^8 is independently a straight or branched alkylene chain; and

each R^{15} is alkyl, $-R^8-OR^5$, $-R^8-C(O)OR^5$, heterocyclyl (optionally substituted by $-R^8-OR^5$), or heterocyclylalkyl (optionally substituted by $-OR^5$); and

R^4 is in the 5-position and is hydrogen or halo.

47. The compound of Claim 46 selected from the group consisting of:

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-(2-(pyrrolidin-1-yl)ethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2-acetoxyethoxy)-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-(methylsulfonyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2-hydroxy-3-(pyrrolidin-1-yl)propoxy)-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-((dimethylamino)sulfonyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2-hydroxy-3-(pyrrolidin-1-yl)propoxy)-5-chlorobenzamide;

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-(methylsulfonyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2-hydroxy-3-(imidazol-1-yl)propoxy)-5-chlorobenzamide; and

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-(methylsulfonyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2-hydroxy-3-methoxypropoxy)-5-chlorobenzamide.

48. The compound of Claim 2 wherein:

A is =N-;

m is 1 to 3;

n is 1;

D is -N(R^5)-C(Z)- (where Z is oxygen and R^5 is hydrogen or alkyl);

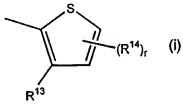
E is -C(Z)-N(R^5)- (where Z is oxygen, R^5 is hydrogen or alkyl, and the nitrogen is attached to the pyridinyl ring);

each R^1 is independently hydrogen, halo or -OR^5;

or two adjacent R^1's together with the carbons to which they are attached form a dioxole ring fused to the phenyl ring wherein the dioxole ring is optionally substituted by alkyl;

R^2 is hydrogen;

R^3 is a radical of the formula (i):



(i)

where r is 1;

R^{13} is halo; and

R^{14} is -C(R^7)H-N(R^{10})R^{11} where:

R^7 is hydrogen; and

R^{10} and R^{11} are each independently hydrogen, alkyl, formyl, -R^8-OR^5, -$S(O)_p$-R^{15} (where p is 0 to 2), -R^8-N(R^5)R^6, -R^8-C(O)OR^5, -C(O)-R^{15}, -C(O)NH_2, -C(S)NH_2, -C(O)-N(R^5)R^{15}, -C(S)-N(R^5)R^{15}, cycloalkyl (optionally substituted by -OR^5), heterocyclyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, haloalkyl, oxo, -OR^5, and -C(O)OR^5), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, haloalkyl, oxo, -OR^5, and -C(O)OR^5); where:

each R^5 and R^6 is hydrogen or alkyl;

each R^8 is independently a straight or branched alkylene chain; and

each R^{15} is alkyl, -R^8-OR^5, -R^8-C(O)OR^5, heterocyclyl (optionally substituted by -R^8-OR^5), or heterocyclylalkyl (optionally substituted by -OR^5); and

R^4 is in the 5-position and is hydrogen or halo.

49. The compound of Claim 48 selected from the group consisting of:

N-(5-chloropyridin-2-yl)-2-[((4-((*N'*-methyl-*N'*-(2-hydroxyethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3,4,5-trimethoxybenzamide;

5-(*N*-(5-chloropyridin-2-yl)amino)carbonyl-6-[4-((*N'*-methyl-*N'*-(oxazolin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl]amino-1,3-benzodioxole;

5-(*N*-(5-chloropyridin-2-yl)amino)carbonyl-6-[4-((*N'*-methyl-*N'*-(2-hydroxyethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl]amino-1,3-benzodioxole; and

5-(*N*-(5-chloropyridin-2-yl)amino)carbonyl-6-[4-((*N'*-(2-methoxyethyl)-*N'*-(oxazolin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl]amino-1,3-benzodioxole.

50. A compound of Claim 2 wherein:

A is -CH-;

m is 1;

n is 1;

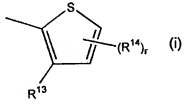
D is -N(R^5)-C(Z)- (where Z is oxygen and R^5 is hydrogen or alkyl);

E is -C(Z)-N(R^5)- (where Z is oxygen, R^5 is hydrogen or alkyl, and the nitrogen is attached to the phenyl ring having the R^4 substituent);

R^1 is alkyl or halo;

R^2 is hydrogen, alkyl, aryl, aralkyl, halo, haloalkyl, cyano, -OR^5, -$S(O)_p$-R^9 (where p is 0 to 2), -C(O)OR^5, -C(O)N(R^5)R^6, -N(R^{10})R^{11}, -C(R^7)H-OR^5, -C(R^7)H-$S(O)_p$-R^9 (where p is 0 to 2), -O-R^8-$S(O)_p$-R^9 (where p is 0 to 2), -C(R^7)H-N(R^5)R^6, -O-R^8-CH(OH)-CH_2-N(R^{10})R^{11}, -O-R^8-N(R^{10})R^{11}, -O-R^8-O-C(O)R^5, -O-R^8-CH(OH)-CH_2-OR^5; O-(R^8-O)$_r$-R^6 (where t is 1 to 6), -O-R^8-C(O)R^5, -O-R^8-C(O)OR^5, -N(R^5)-R^8-N(R^{10})R^{11}, -$S(O)_p$-R^8-N(R^5)R^6 (where p is 0 to 2), -$S(O)_p$-R^8-C(O)OR^5 (where p is 0 to 2), -N(R^5)-CH(R^{12})-C(O)OR^5;

R^3 is a radical of formula (i):



(i)

where:

r is 1 or 2;

R^{13} is hydrogen, alkyl, halo, haloalkyl, -N(R^5)R^6, -C(R^7)H-N(R^5)R^6, -OR^5, -$S(O)_p$-R^8-N(R^5)R^6 (where p is 0 to 2) or heterocyclylalkyl (where the heterocyclic ring is optionally substituted by one or more substituents selected from the group

consisting of alkyl, halo, aralkyl, nitro and cyano); and

each R^{14} is independently hydrogen, alkyl, halo, formyl, acetyl, $-N(R^{10})R^{11}$,

$-C(R^7)H-N(R^{10})R^{11}$, $-C(R^7)H-N^{\oplus}(R^9)(R^{16})_2$, $-N(R^5)-R^8-C(O)OR^5$,

$-C(R^7)H-N(R^5)-R^8-C(O)OR^5$, $-C(O)OR^5$, $-OR^5$, $-C(R^7)H-OR^5$, $-S(O)_p-R^{15}$ (where p is 0 to 2), $-C(R^7)H-S(O)_p-R^{15}$ (where p is 0 to 2), $-S(O)_p-N(R^5)R^6$ (where p is 0 to 2), $-C(O)N(R^5)R^6$, $-C(R^7)H-N(R^5)-(R^8-O)_t-R^5$ (where t is 1 to 6), $-C(R^7)H-O-(R^8-O)_t-R^5$ (where t is 1 to 6), $-O-R^8-CH(OH)-CH_2-OR^5$, $-C(R^7)H-O-R^8-CH(OH)-CH_2-OR^5$, $-C(R^7)H-N(R^5)-R^8-[CH(OH)]_t-CH_2-OR^5$ (where t is 1 to 6), $-C(R^7)H-N(R^5)-S(O)_2-N(R^{10})R^{11}$, $-C(R^7)H-N(R^{10})-C(NR^{17})-N(R^{10})R^{11}$, or $-C(R^7)H-N(R^{10})-C(NR^{17})-R^{10}$;

R^4 is halo;

R^5 and R^6 are each independently hydrogen, alkyl, aryl or aralkyl;

R^7 is hydrogen or alkyl;

each R^8 is independently a straight or branched alkylene or alkylidene chain;

each R^9 is independently alkyl, aryl or aralkyl;

R^{10} and R^{11} are each independently hydrogen, alkyl, aryl, aralkyl, formyl, $-OR^5$, $-R^8-OR^5$, $-S(O)_p-R^{15}$ (where p is 0 to 2), $-R^8-N(R^5)R^6$, $-R^8-C(O)OR^5$, $-C(O)-R^{15}$, $-C(O)NH_2$, $-C(S)NH_2$, $-C(O)-N(R^5)R^{15}$, $-C(S)-N(R^5)R^{15}$, cycloalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, halo and $-OR^5$), heterocyclyl (optionally substituted by alkyl, aryl, aralkyl, halo, haloalkyl, oxo, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^8$ or $-C(O)N(R^5)R^8$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, oxo, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ and $-C(O)N(R^5)R^6$);

or R^{10} and R^{11} together with the nitrogen to which they are attached form a *N*-heterocyclic ring containing zero to three additional hetero atoms, where the *N*-heterocylic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, oxo, $=N(R^{17})$, $-OR^5$, $-C(O)OR^5$, $-R^8-C(O)OR^5$, $-N(R^5)R^6$, $-R^8-N(R^5)R^6$, $-C(O)R^5$, $-C(O)-(R^8-O)_t-R^5$ (where t is 1 to 6), and $-(R^8-O)_t-R^5$ (where t is 1 to 6);

R^{12} is a side chain of an α-amino acid;

each R^{15} is independently alkyl, haloalkyl, aryl, aralkyl, $-R^8-OR^5$, $-R^8-N(R^5)R^6$, $-R^8-C(O)OR^5$, heterocyclyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$, and $-C(O)N(R^5)R^6$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-C(O)OR^5$,

$-N(R^5)R^6$, and $-C(O)N(R^5)R^6$);

or R^5 and R^{15} together with the nitrogen to which they are attached form a *N*-heterocyclic ring containing zero to three additional hetero atoms, where the *N*-heterocyclic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, amino, monoalkylamino, dialkylamino, $-OR^5$, $-C(O)OR^5$, aminocarbonyl, monoalkylaminocarbonyl, and dialkylaminocarbonyl; and

each R^{16} is independently alkyl, aryl, aralkyl, $-R^8-OR^5$, $-R^8-N(R^5)R^6$, cycloalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, halo and $-OR^5$), heterocyclyl (optionally substituted by alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ or $-C(O)N(R^5)R^6$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ and $-C(O)N(R^5)R^6$), or

both R^{16}s together with the nitrogen to which they are attached (and wherein the R^9 substituent is not present) form an aromatic *N*-heterocyclic ring containing zero to three additional hetero atoms, where the *N*-heterocylic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, $-OR^5$, $-C(O)OR^5$, $-R^8-C(O)OR^5$, $-N(R^5)R^6$, $-R^8-N(R^5)R^6$, $-C(O)R^5$, $-C(O)-(R^8-O)_t-R^5$ (where t is 1 to 6), and $-(R^8-O)_t-R^5$ (where t is 1 to 6).

51. A compound of Claim 50 wherein:

D is -N(H)-C(O)-;

E is -C(O)-N(H)-;

R^1 is halo;

R^2 is hydrogen, $-OR^5$, $-N(R^{10})R^{11}$, $-O-R^8-S(O)_p-R^9$ (where p is 0 to 2), $-O-R^8-N(R^{10})R^{11}$, $-O-R^8-O-C(O)R^5$ or $-O-R^8-C(O)OR^5$ where:

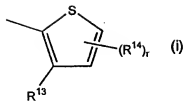
each R^5 is hydrogen or alkyl;

each R^8 is independently a straight or branched alkylene chain;

R^9 is alkyl;

R^{10} and R^{11} together with the nitrogen to which they are attached form a *N*-heterocyclic ring containing zero to three additional hetero atoms;

R^3 is a radical of formula (i):



where:

r is 1;

R^{13} is halo; and

R^{14} is in the 4-position and is $-C(R^7)H-N(R^{10})R^{11}$ where:

R^7 is hydrogen or alkyl; and

R^{10} and R^{11} are each independently hydrogen, alkyl, $-R^8-OR^5$ or heterocyclyl;

or R^{10} and R^{11} together with the nitrogen to which they are attached form a piperazine ring optionally substituted by alkyl; and

R^4 is chloro.

52. The compound of Claim 51 selected from the group consisting of:

N-(4-chlorophenyl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-hydroxy-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-5-fluorobenzamide;

N-(4-chlorophenyl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(ethoxycarbonyl)methoxy-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-((acetoxy)ethoxy)-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(2-(morpholin-4-yl)ethoxy)-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-((methylthio)methoxy)-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(3-(morpholin-4-yl)propoxy)-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((4-((*N'*-methyl-*N'*-(2-hydroxyethyl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-(morpholin-4-yl)-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((4-((*N'*-methyl-*N'*-(oxazolin-2-yl)amino)methyl)-3-chlorothiophen-2-

yl)carbonyl)amino]-3-(morpholin-4-yl)-5-chlorobenzamide; and

N-(4-chlorophenyl)-2-[((4-((*N'*-methyl-*N'*-(oxazolin-2-yl)amino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide.

53. The compound of Claim 50 wherein:

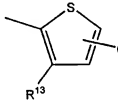
D is -N(H)-C(O)-;

E is -C(O)-N(H)-;

R^1 is methyl or chloro;

R^2 is hydrogen or $-OR^5$;

R^3 is a radical of formula (i):



(i)

where:

r is 1 or 2;

R^{13} is alkyl, halo, OR^5 (where R^5 is alkyl) or heterocyclylalkyl (where the heterocyclic ring is optionally substituted by alkyl); and

each R^{14} is independently hydrogen, alkyl, halo, formyl, $-N(R^{10})R^{11}$, $-C(R^7)H-N(R^{10})R^{11}$, $-C(R^7)H-N^{\oplus}(R^9)(R^{16})_2$, $-C(O)OR^5$, $-C(R^7)H-OR^5$, $-S(O)_p-R^{15}$ (where p is 0 to 2), $-C(R^7)H-S(O)_p-R^{15}$ (where p is 0 to 2), $-C(O)N(R^5)R^6$, $-C(R^7)H-N(R^5)-(R^8-O)_t-R^5$ (where t is 1 to 6), $-C(R^7)H-O-(R^8-O)_t-R^5$ (where t is 1 to 6), $-C(R^7)H-O-R^8-CH(OH)-CH_2-OR^5$, or $-C(R^7)H-N(R^5)-R^8-[CH(OH)]_t-CH_2-OR^5$ (where t is 1 to 6);

R^4 is halo;

R^5 and R^6 are each independently hydrogen or alkyl;

each R^7 is independently hydrogen or alkyl;

each R^8 is independently a straight or branched alkylene chain;

R^9 is alkyl;

R^{10} and R^{11} are each independently hydrogen, alkyl, aryl, aralkyl, formyl, $-OR^5$, $-R^8-OR^5$, $-S(O)_p-R^{15}$ (where p is 0 to 2), $-R^8-N(R^5)R^6$, $-R^8-C(O)OR^5$, $-C(O)-R^{15}$, $-C(O)NH_2$, $-C(S)NH_2$, $-C(O)-N(R^5)R^{15}$, $-C(S)-N(R^5)R^{15}$, heterocyclyl (optionally substituted by alkyl, aryl, aralkyl,

halo, haloalkyl, oxo, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ or $-C(O)N(R^5)R^6$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, oxo, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ and $-C(O)N(R^5)R^6$);

or R^{10} and R^{11} together with the nitrogen to which they are attached form a *N*-heterocyclic ring containing zero to three additional hetero atoms, where the *N*-heterocylic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, oxo, $-N(R^5)R^6$, $-R^8-C(O)OR^5$, $-C(O)R^5$, and $-C(O)-(R^8-O)_t-R^5$ (where t is 1 to 6);

R^{15} is alkyl, haloalkyl, aryl, aralkyl, $-R^8-OR^5$, $-N(R^5)R^6$, $-R^8-N(R^5)R^8$, $-R^8-C(O)OR^5$, heterocyclyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$, and $-C(O)N(R^5)R^6$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$, and $-C(O)N(R^5)R^6$);

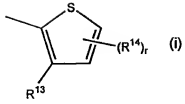
or R^5 and R^{15} together with the nitrogen to which they are attached form a *N*-heterocyclic ring containing zero to three additional hetero atoms, where the *N*-heterocyclic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, amino, monoalkylamino, dialkylamino, $-OR^5$, $-C(O)OR^5$, aminocarbonyl, monoalkylaminocarbonyl, and dialkylaminocarbonyl; and

each R^{16} is independently alkyl, aryl, aralkyl, $-R^8-OR^5$, $-R^8-N(R^5)R^8$, cycloalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, halo and $-OR^5$), heterocyclyl (optionally substituted by alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ or $-C(O)N(R^5)R^8$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ and $-C(O)N(R^5)R^6$), or

both R^{16}'s together with the nitrogen to which they are attached (and wherein the R^9 substituent is not present) form an aromatic *N*-heterocyclic ring containing zero to three additional hetero atoms, where the *N*-heterocylic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, $-OR^5$, $-C(O)OR^5$, $-R^8-C(O)OR^5$, $-N(R^5)R^6$, $-R^8-N(R^5)R^6$, $-C(O)R^5$, $-C(O)-(R^8-O)_t-R^5$ (where t is 1 to 6), and $-(R^8-O)_t-R^5$ (where t is 1 to 6).

54. The compound of Claim 53 wherein:

R^3 is a radical of formula (i):



where:

r is 1 or 2;

R^{13} is halo, alkyl or 4-methylpiperazin-1-yl, and

each R^{14} is independently hydrogen or $-C(R^7)H-N(R^{10})R^{11}$ where:

R^7 is hydrogen or alkyl;

R^{10} and R^{11} are each independently hydrogen, alkyl, aryl, aralkyl, formyl, $-OR^5$, $-R^8-OR^5$, $-S(O)_p-R^{15}$ (where p is 0 to 2), $-R^8-N(R^5)R^6$, $-R^8-C(O)OR^5$, $-C(O)-R^{15}$, $-C(O)NH_2$, $-C(S)NH_2$, $-C(O)-N(R^5)R^{15}$, $-C(S)-N(R^5)R^{15}$, heterocyclyl (optionally substituted by alkyl, aryl, aralkyl, halo, haloalkyl, oxo, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ or $-C(O)N(R^5)R^6$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, oxo, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ and $-C(O)N(R^5)R^6$) where:

each R^5 and R^6 are independently hydrogen or alkyl;

each R^8 is independently a straight or branched alkylene chain; and

each R^{15} is alkyl, haloalkyl, aryl, aralkyl, $-R^8-OR^5$, $-R^8-N(R^5)R^6$, $-R^8-C(O)OR^5$, heterocyclyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$, and $-C(O)N(R^5)R^6$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$, and $-C(O)N(R^5)R^6$).

55. The compound of Claim 54 selected from the group consisting of:

N-(4-chlorophenyl)-2-[((3-methylthiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-((4-methylpiperazin-1-yl)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((5-((dimethylamino)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-5-(*N*'-methyl-*N*'-(2-hydroxyethyl)amino)methylthiophen-2-

yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-5-(*N'*-methyl-*N'*-(ethoxycarbonylmethyl)amino)methylthiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-5-(*N'*-methyl-*N'*-(carboxymethyl)amino)methylthiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-5-(*N'*,*N'*-di(2-hydroxyethyl)amino)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-5-(((*N'*-(3-dimethylaminophenyl)amino)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-4,5-di((*n*-propyl)aminomethyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-5-((*N'*-methyl-*N'*-(2-dimethylaminoethyl)amino)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-4-((*N'*-methyl-*N'*-(2-hydroxyethyl)amino)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-4-((*N'*-methyl-*N'*-(ethoxycarbonylmethyl)amino)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-4-((*N'*-methyl-*N'*-(2-dimethylaminoethyl)amino)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-4-((*N'*-(3-(imidazol-1-yl)propyl)amino)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-4-((*N'*-methyl-*N'*-(3-(dimethylamino)propyl)amino)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-4-((*N'*-(2-methylpropyl)amino)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-4-((*N'*-methyl-*N'*-(1-methylpiperidin-4-yl)amino)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-4-((*N'*-(2-(morpholin-4-yl)ethyl)amino)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-4-((*N'*-methyl-*N'*-hydroxyamino)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

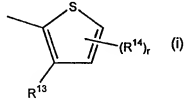
N-(4-chlorophenyl)-2-[((3-chloro-4-((*N'*-methyl-*N'*-(2-diethylaminoethyl)amino)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-4-((*N'*-(2-hydroxyethyl)-*N'*-(2-(morpholin-4-yl)ethyl)amino)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide; and

N-(4-chlorophenyl)-2-[((3-chloro-4-((*N*'-methyl-*N*'-(2-(pyrrolidin-1-yl)ethyl)amino)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide.

56. The compound of Claim 53 wherein:

R^3 is a radical of formula (i):



(i)

where:

r is 1 or 2;

R^{13} is halo or alkyl, and

each R^{14} is independently hydrogen, alkyl or $-C(R^7)H-N(R^{10})R^{11}$ where:

R^7 is hydrogen or alkyl; and

R^{10} and R^{11} together with the nitrogen to which they are attached form a *N*-heterocyclic ring containing zero to three additional hetero atoms, where the *N*-heterocylic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, oxo, $-N(R^5)R^6$, $-R^8-C(O)OR^5$, $-C(O)R^5$, and $-C(O)-(R^8-O)_t-R^5$ (where t is 1 to 6) where

each R^5 is hydrogen or alkyl; and

R^8 is a straight or branched alkylene chain.

57. The compound of Claim 56 selected from the group consisting of:

N-(4-chlorophenyl)-2-[((4-methyl-3-chlorothiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-5-((4-(carboxymethyl)piperazin-1-yl)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((5-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-5-((4-(ethoxycarbonylmethyl)piperazin-1-yl)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-5-(thiomorpholin-4-yl)methylthiophen-2-yl)carbonyl)amino]-5-

chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-5-(morpholin-4-yl)methylthiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-5-(1-(oxo)thiomorpholin-4-yl)methylthiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-5-((4-(((2-(2-methoxyethoxy)ethoxy)methyl)carbonyl)piperazin-1-yl)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((4-(morpholin-4-yl)methyl-3-chlorothiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-5-(1,1,4-tri(oxo)thiomorpholin-4-yl)methylthiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-4-(thiomorpholin-4-yl)methylthiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-5-((imidazol-1-yl)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-5-methyl-4-((4-methylpiperazin-1-yl)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-4-methyl-5-((4-methylpiperazin-1-yl)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-4-((4*H*-1,2,4-triazol-1-yl)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-4-((imidazol-1-yl)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-4-((tetrazol-1-yl)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-4-((tetrazol-2-yl)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-4-((pyrazol-1-yl)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-4-((1,2,3-triazol-1-yl)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-4-((4-(2-(2-hydroxyethoxy)ethyl)piperazin-1-yl)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-4-((1,2,3-triazol-2-yl)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-4-((4-ethylpiperazin-1-yl)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

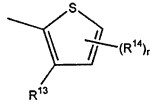
N-(4-chlorophenyl)-2-[((3-chloro-4-((4-oxomorpholin-4-yl)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-4-((4-acetylpiperazin-1-yl)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide; and

N-(4-chlorophenyl)-2-[((4-((2-aminoimidazol-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide.

58. The compound of Claim 53 wherein:

R^3 is a radical of formula (i):



(i)

where:

r is 1 or 2;

R^{13} is halo or alkyl, and

each R^{14} is independently $-C(R^7)H-S(O)_p-R^{15}$ where:

p is 0 to 2;

R^7 is hydrogen or alkyl; and

R^{15} is alkyl, $-R^8-N(R^5)R^6$ or $-R^8-C(O)OR^5$ where:

R^5 and R^6 are each independently hydrogen or alkyl; and

each R^8 is independently a straight or branched alkylene chain.

59. The compound of Claim 58 selected from the group consisting of:

N-(4-chlorophenyl)-2-[((3-chloro-5-((methylthio)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-5-(((methoxycarbonylmethyl)thio)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-5-(((methoxycarbonylmethyl)sulfinyl)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-5-((methylsulfinyl)methyl)thiophen-2-yl)carbonyl)amino]-5-

chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-5-(((carboxymethyl)thio)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-5-((methylsulfonyl)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-5-(((2-(dimethylamino)ethyl)thio)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-5-(((2-(dimethylamino)ethyl)sulfinyl)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-4-((methylthio)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-4-(((methoxycarbonylmethyl)thio)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

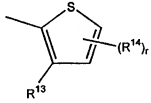
N-(4-chlorophenyl)-2-[((3-chloro-4-(((2-(dimethylamino)ethyl)thio)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-4-((methylsulfonyl)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide; and

N-(4-chlorophenyl)-2-[((3-chloro-4-((methylsulfinyl)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide.

60. The compound of Claim 53 wherein:

R^3 is a radical of formula (i):



(i)

where:

r is 1 or 2;

R^{13} is halo or alkyl, and

each R^{14} is independently formyl, $-N(R^{10})R^{11}$, $-C(O)OR^5$, $-C(R^7)H-OR^5$ or $-C(O)N(R^5)R^6$ where:

R^5 and R^6 are each independently hydrogen or alkyl;

R^7 is hydrogen or alkyl; and

R^{10} and R^{11} are independently hydrogen or alkyl.

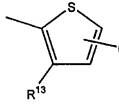
61. The compound of Claim 60 selected from the group consisting of:

N-(4-chlorophenyl)-2-[((3-chloro-5-carboxythiophen-2-yl)carbonyl)amino]-5-chlorobenzamide; and

N-(4-chlorophenyl)-2-[((3-chloro-4-(hydroxymethyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide.

62. The compound of Claim 53 wherein:

R^3 is a radical of formula (i):



(i)

where:

r is 1 or 2;

R^{13} is alkyl, halo or $-OR^5$ (where R^5 is alkyl), and

each R^{14} is independently hydrogen, halo, $-C(R^7)H\text{-}N^{\oplus}(R^5)(R^{16})_2$, $-S(O)_p\text{-}R^{15}$,

$-C(R^7)H\text{-}N(R^5)\text{-}(R^8\text{-}O)_t\text{-}R^5$ (where t is 1 to 6), $-C(R^7)H\text{-}O\text{-}(R^8\text{-}O)_t\text{-}R^5$ (where t is 1 to 6), $-C(R^7)H\text{-}O\text{-}R^8\text{-}CH(OH)\text{-}CH_2\text{-}OR^5$, or $-C(R^7)H\text{-}N(R^5)\text{-}R^8\text{-}[CH(OH)]_t\text{-}CH_2\text{-}OR^5$ (where t is 1 to 6) where:

R^5 and R^6 are independently hydrogen or alkyl;

R^7 is hydrogen or alkyl;

each R^8 is independently a straight or branched alkylene chain;

R^{10} and R^{11} are independently hydrogen, alkyl or $-R^8\text{-}OR^5$ where R^8 is a straight or branched alkylene chain and R^5 is hydrogen or alkyl; and

R^{15} is alkyl or $-N(R^5)R^6$; and

each R^{16} is independently alkyl, aryl, aralkyl, $-R^8\text{-}OR^5$, $-R^8\text{-}N(R^5)R^5$, cycloalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, halo and $-OR^5$), heterocyclyl (optionally substituted by alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ or $-C(O)N(R^5)R^6$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo,

haloalkyl, -OR^5, -$C(O)OR^5$, -$N(R^5)R^6$ and -$C(O)N(R^5)R^6$), or both R^{16}s together with the nitrogen to which they are attached (and wherein the R^9 substituent is not present) form an aromatic *N*-heterocyclic ring containing zero to three additional hetero atoms, where the *N*-heterocylic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, -OR^5, -$C(O)OR^5$, -R^8-$C(O)OR^5$, -$N(R^5)R^6$, -R^8-$N(R^5)R^6$, -$C(O)R^5$, -$C(O)$-$(R^8$-$O)_t$-R^5 (where t is 1 to 6), and -$(R^8$-$O)_t$-R^5 (where t is 1 to 6).

63. The compound of Claim 62 selected from the group consisting of:

N-(4-chlorophenyl)-2-[((3-chloro-4-((*N',N'*-dimethyl-*N'*-(2-hydroxyethyl)ammonio)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-4-((((2-hydroxyethoxy)ethyl)amino)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-4-((2-(2-methoxyethoxy)ethoxy)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-4-((2-(2-(2-methoxyethoxy)ethoxy)ethoxy)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-4-((2-methoxyethoxy)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-4-((*N',N'*-dimethyl-*N'*-(3-hydroxypropyl)ammonio)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-4-((*N'*-methyl-*N'*-(2,3-dihydroxypropyl)amino)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-4-((*N'*-methyl-*N'*-(2,3,4,5,6-pentahydroxyhexyl)amino)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-4-((*N'*-methyl-*N'*-(2-(hydroxyethoxy)ethyl)amino)methyl)thiophen-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-4-(methylsulfonyl)thiophen-2-yl)carbonyl)amino]-5-methylbenzamide;

N-(4-chlorophenyl)-2-[((3-chlorothiophen-2-yl)carbonyl)amino]-5-methylbenzamide;

N-(4-chlorophenyl)-2-[((3-bromothiophen-2-yl)carbonyl)amino]-5-methylbenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-4-((1-methylethyl)sulfonyl)thiophen-2-yl)carbonyl)amino]-5-methylbenzamide;

N-(4-chlorophenyl)-2-[((4-(methylamino)sulfonyl-3-methylthiophen-2-yl)carbonyl)amino]-5-

methylbenzamide; and

N-(4-chlorophenyl)-2-[((3-methoxythiophen-2-yl)carbonyl)amino]-5-methylbenzamide.

64. The compound of Claim 2 wherein:

A is -CH- or =N-;

m is 1 to 3;

n is 1 to 4;

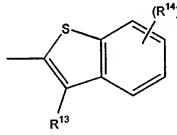
D is -N(H)-C(O)- or -N(H)-CH_2-;

E is -C(O)-N(H)-; (where the nitrogen atom is bonded to the aromatic ring containing the R^4 substituent);

each R^1 is independently hydrogen, alkyl, aryl, aralkyl, halo, haloalkyl, cyano, $-OR^5$, $-S(O)_p-R^9$ (where p is 0 to 2), $-C(O)OR^5$, $-C(O)N(R^5)R^6$, $-N(R^5)R^6$, -O-C(O)R^5, or $-N(R^5)-CH(R^{12})-C(O)OR^5$;

R^2 is hydrogen, alkyl, aryl, aralkyl, halo, haloalkyl, cyano, $-OR^5$, $-S(O)_p-R^9$ (where p is 0 to 2), $-C(O)OR^5$, $-OC(O)-R^5$, $-C(O)N(R^5)R^6$, $-N(R^{10})R^{11}$, $-C(R^7)H-OR^5$, $-C(R^7)H-S(O)_p-R^9$ (where p is 0 to 2), $-O-R^8-S(O)_p-R^9$ (where p is 0 to 2), $-C(R^7)H-N(R^5)R^6$, $-O-R^8-CH(OH)-CH_2-N(R^{10})R^{11}$ $-O-R^8-N(R^{10})R^{11}$, $-O-R^8-O-C(O)R^5$, $-O-R^8-CH(OH)-CH_2-OR^5$; $-O-(R^8-O)_t-R^5$ (where t is 1 to 6), $-O-R^8-C(O)R^5$, $-O-R^8-C(O)OR^5$, $-N(R^5)-R^8-N(R^{10})R^{11}$, $-S(O)_p-R^8-N(R^5)R^6$ (where p is 0 to 2), $-S(O)_p-R^8-C(O)OR^5$ (where p is 0 to 2), or $-N(R^5)-CH(R^{12})-C(O)OR^5$;

R^3 is a radical of formula (ii):



(ii)

where v is 1 to 4;

R^{13} is hydrogen, alkyl, halo, haloalkyl, $-N(R^5)R^6$, $-C(R^7)H-N(R^5)R^6$, $-OR^5$, $-S(O)_p-R^8-N(R^5)R^6$ (where p is 0 to 2) or heterocyclylalkyl (where the heterocyclic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, halo, aralkyl, nitro and cyano); and

each R^{14} is independently hydrogen, alkyl, halo, formyl, acetyl, $-N(R^{10})R^{11}$,

$-C(R^7)H-N(R^{10})R^{11}$, $-C(R^7)H-N^{\oplus}(R^9)(R^{16})_2$, $-N(R^5)-R^8-C(O)OR^5$,

$-C(R^7)H-N(R^5)-R^8-C(O)OR^5$, $-C(O)OR^5$, $-OR^5$, $-C(R^7)H-OR^5$, $-S(O)_p-R^{15}$ (where p is 0 to 2), $-C(R^7)H-S(O)_p-R^{15}$ (where p is 0 to 2), $-S(O)_p-N(R^5)R^6$ (where p is 0 to 2), $-C(O)N(R^5)R^6$, $-C(R^7)H-N(R^5)-(R^8-O)_t-R^5$ (where t is 1 to 6), $-C(R^7)H-O-(R^8-O)_t-R^5$ (where t is 1 to 6), $-O-R^8-CH(OH)-CH_2-OR^5$, $-C(R^7)H-O-R^8-CH(OH)-CH_2-OR^5$, $-C(R^7)H-N(R^5)-R^8-[CH(OH)]_t-CH_2-OR^5$ (where t is 1 to 6), $-C(R^7)H-N(R^5)-S(O)_2-N(R^{10})R^{11}$, $-C(R^7)H-N(R^{10})-C(NR^{17})-N(R^{10})R^{11}$, or $-C(R^7)H-N(R^{10})-C(NR^{17})-R^{10}$;

each R^4 is independently hydrogen, alkyl, halo, haloalkyl, cyano, nitro, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$, $-C(O)N(R^5)R^6$, or $-R^8-N(R^5)R^6$;

R^5 and R^6 are each independently hydrogen, alkyl, aryl or aralkyl;

each R^7 is independently hydrogen or alkyl;

each R^8 is independently a straight or branched alkylene or alkylidene chain;

each R^9 is independently alkyl, aryl or aralkyl;

R^{10} and R^{11} are each independently hydrogen, alkyl, aryl, aralkyl, formyl, $-OR^5$, $-R^8-OR^5$, $-S(O)_p-R^{15}$ (where p is 0 to 2), $-R^8-N(R^5)R^6$, $-R^8-C(O)OR^5$, $-C(O)-R^{15}$, $-C(O)NH_2$, $-C(S)NH_2$, $-C(O)-N(R^5)R^{15}$, $-C(S)-N(R^5)R^{15}$, cycloalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, halo and $-OR^5$), heterocyclyl (optionally substituted by alkyl, aryl, aralkyl, halo, haloalkyl, oxo, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ or $-C(O)N(R^5)R^6$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, oxo, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ and $-C(O)N(R^5)R^6$);

or R^{10} and R^{11} together with the nitrogen to which they are attached form a *N*-heterocyclic ring containing zero to three additional hetero atoms, where the *N*-heterocylic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, oxo, $=N(R^{17})$, $-OR^5$, $-C(O)OR^5$, $-R^8-C(O)OR^5$, $-N(R^5)R^6$, $-R^8-N(R^5)R^6$, $-C(O)R^5$, $-C(O)-(R^8-O)_t-R^5$ (where t is 1 to 6), and $-(R^8-O)_t-R^5$ (where t is 1 to 6);

R^{12} is a side chain of an α-amino acid;

R^{15} is alkyl, haloalkyl, aryl, aralkyl, $-R^8-OR^5$, $-N(R^5)R^6$, $-R^8-N(R^5)R^6$, $-R^8-C(O)OR^5$, heterocyclyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$, and $-C(O)N(R^5)R^6$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$, and $-C(O)N(R^5)R^6$);

or R^5 and R^{15} together with the nitrogen to which they are attached form a *N*-heterocyclic ring containing zero to three additional hetero atoms, where the *N*-heterocyclic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, amino, monoalkylamino, dialkylamino, $-OR^5$, $-C(O)OR^5$, aminocarbonyl, monoalkylaminocarbonyl, and dialkylaminocarbonyl; and

each R^{16} is independently alkyl, aryl, aralkyl, $-R^8-OR^5$, $-R^8-N(R^5)R^6$, cycloalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, halo and $-OR^5$), heterocyclyl (optionally substituted by alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ or $-C(O)N(R^5)R^6$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ and $-C(O)N(R^5)R^6$), or

both R^{16}'s together with the nitrogen to which they are attached (and wherein the R^9 substituent is not present) form an aromatic *N*-heterocyclic ring containing zero to three additional hetero atoms, where the *N*-heterocyclic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, $-OR^5$, $-C(O)OR^5$, $-R^8-C(O)OR^5$, $-N(R^5)R^6$, $-R^8-N(R^5)R^6$, $-C(O)R^5$, $-C(O)-(R^8-O)_t-R^5$ (where t is 1 to 6), and $-(R^8-O)_t-R^5$ (where t is 1 to 6); and

each R^{17} is independently hydrogen, alkyl, aryl, aralkyl, cyano, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-R^8-C(O)OR^5$, $-C(O)-N(R^5)R^6$, or $-R^8-C(O)-N(R^5)R^6$.

65. The compound of Claim 64 selected from the group consisting of:

N-phenyl-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-5-methylbenzamide;

N-(pyridin-3-yl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-5-methylbenzamide;

N-(pyridin-2-yl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-5-methylbenzamide;

N-(4-methoxyphenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-5-methylbenzamide;

N-(3-fluorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-5-methylbenzamide;

N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-5-methylbenzamide;

N-(4-bromophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-5-methylbenzamide;

N-(5-chloropyridin-2-yl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-5-methylbenzamide;

N-(3-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-5-methylbenzamide;

N-(3-methylphenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-5-methylbenzamide;

N-(4-chloro-2-methylphenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-5-methylbenzamide;

N-(4-cyanophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-5-methylbenzamide;

N-(4-fluorophenyl)-2-[((benzo[*b*]thien-2-yl)carbonyl)amino]-5-methylbenzamide;

N-(4-fluorophenyl)-2-[((3-methylbenzo[*b*]thien-2-yl)carbonyl)amino]-5-methylbenzamide;
N-(4-chlorophenyl)-2-[((3-methoxybenzo[*b*]thien-2-yl)carbonyl)amino]-5-methylbenzamide;
N-(4-fluorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]benzamide;
N-(4-fluorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-5-methoxybenzamide;
N-(4-bromophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-5-chlorobenzamide;
N-phenyl-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-3-methylbenzamide;
N-(4-fluorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-5-(pyrrolidin-1-yl)methylbenzamide;
N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-4-(trifluoromethyl)benzamide;
N-(4-fluorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-5-(dimethylamino)methylbenzamide;
N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-5-(4-methylpiperazin-1-yl)benzamide;
N-(4-fluorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-5-(amino)methylbenzamide;
N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-5-hydroxybenzamide;
N-phenyl-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-4,5-dimethoxybenzamide;
N-phenyl-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-4,5-dihydroxybenzamide;
N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-5-fluorobenzamide;
N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-3-chlorobenzamide;
N-phenyl-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-3-methoxybenzamide;
N-phenyl-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-3-hydroxybenzamide;
N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-4-fluorobenzamide;
N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-4-chlorobenzamide;
N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-3-methoxybenzamide;
N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-6-fluorobenzamide;
N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-3-hydroxybenzamide;
N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-4-methylbenzamide;
N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-3-(ethoxycarbonyl)methoxybenzamide;
N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-4,5-dihydroxybenzamide;
N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-4,5-dimethoxybenzamide;
N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]benzamide;
N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-5-aminobenzamide;
N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-4-methyl-5-

chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-3-methoxy-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-3-methylbenzamide;

N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-3-methyl-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-4-fluoro-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-3-hydroxy-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-4,5-difluorobenzamide;

N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-4-(*N*'-methyl-*N*'-(3-(dimethylamino)propylamino-5-fluorobenzamide;

N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-4-(4-methylpiperazin-1-yl)-5-fluorobenzamide;

N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-4-((3-(4-methylpiperazin-1-yl)propyl)amino)-5-fluorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-6-methylbenzo[*b*]thien-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-methylbenzo[*b*]thien-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-(dimethylamino)methylbenzo[*b*]thien-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-6-(dimethylamino)methylbenzo[*b*]thien-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-(4-methylpiperazin-1-yl)methylbenzo[*b*]thien-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-6-(4-methylpiperazin-1-yl)methylbenzo[*b*]thien-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-6-(4-(carboxymethyl)piperazin-1-yl)methylbenzo[*b*]thien-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chloro-6-((methoxycarbonyl)methylthio)methylbenzo[*b*]thien-2-yl)carbonyl)amino]-5-chlorobenzamide;

N-(4-chlorophenyl)-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-5-chlorobenzamide;

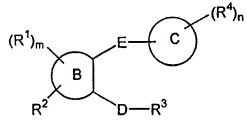
N-(5-chloropyridin-2-yl)-2-[((4-((4-methylpiperazin-1-yl)methyl)-3-chlorothiophen-2-yl)carbonyl)amino]-3-chloro-5-(*N*'-methyl-*N*'-(ethoxycarbonyl)methylamino)benzamide;

N-(5-chloropyridin-2-yl)-2-[((4-(*N*'-methyl-*N*'-(2-(dimethylamino)ethyl)amino)-3-chlorothiophen-2-yl)carbonyl)amino]-3-chloro-5-(*N*'-methyl-*N*'-(ethoxycarbonyl)methylamino)benzamide;

N-phenyl-2-[((3-chlorobenzo[*b*]thien-2-yl)carbonyl)amino]-5-hdyroxy-4-((1,1-dimethylethyl)carbonyl)oxybenzamide; and

N'-(4-chlorophenyl)-2-((3-methylbenzo[*b*]thien-2yl)methyl)amino-5-benzamide.

66. A pharmaceutical composition useful in treating a human having a disease-state characterized by thrombotic activity, which composition comprises a therapeutically effective amount of a compound of formula (III):

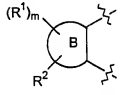


(III)

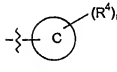
wherein

m is 1 to 3;

n is 1 to 5;



is an aryl or a heterocyclic ring substituted by R^2 and one or more R^1 groups;



is an aryl or a heterocyclic ring substituted by one or more R^4 groups;

D and E are independently a linker selected from the group consisting of -N(R^5)-C(X)-; -R^8-N(R^5)-C(X)-; -N(R^5)-C(X)-R^8-; -R^8-N(R^5)-C(X)-R^8- ; -N(R^5)-S(O)$_p$-; -R^8-N(R^5)-S(O)$_p$-; -N(R^5)-S(O)$_p$-R^8- ; and -R^8-N(R^5)-S(O)$_p$-R^8- (where p is 0 to 2; X is oxygen, sulfur or H_2) where D and E can be attached to the B ring having the R^1 and R^2 substituents by either terminus of the linker;

each R^1 is independently hydrogen, alkyl, aryl, aralkyl, halo, haloalkyl, cyano, -OR^5, -S(O)$_p$-R^9 (where p is 0 to 2), -C(O)OR^5, -C(O)N(R^5)R^6, -N(R^5)R^6, -O-C(O)R^5, -N(R^5)-CH(R^{12})-C(O)OR^5, heterocyclyl (optionally substituted by alkyl, aryl, aralkyl, halo, haloalkyl, oxo, -OR^5, -C(O)OR^5, -N(R^5)R^6 or -C(O)N(R^5)R^6) or heterocyclylalkyl (optionally

substituted by alkyl, aryl, aralkyl, halo, haloalkyl, oxo, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ or $-C(O)N(R^5)R^6$);

R^2 is hydrogen, alkyl, aryl, aralkyl, halo, haloalkyl, cyano, $-OR^5$, $-S(O)_p-R^9$ (where p is 0 to 2), $-C(O)OR^5$, $-C(O)N(R^5)R^6$, $-N(R^{10})R^{11}$, $-C(R^7)H-N(R^{10})R^{11}$, $-C(R^7)H-R^8-N(R^{10})R^{11}$, $-C(R^7)H-OR^5$, $-C(R^7)H-R^8-OR^5$, $-C(R^7)H-S(O)_p-R^9$ (where p is 0 to 2), $-C(R^7)H-R^8-S(O)_p-R^9$ (where p is 0 to 2), $-O-R^8-S(O)_p-R^9$ (where p is 0 to 2), $-C(R^7)H-N(R^5)R^6$, $-C(R^7)H-R^8-N(R^5)R^6$, $-O-R^8-CH(OH)-CH_2-N(R^{10})R^{11}$, $-O-R^8-N(R^{10})R^{11}$, $-O-R^8-O-C(O)R^5$, $-O-R^8-CH(OH)-CH_2-OR^5$, $-O-(R^8-O)_t-R^5$ (where t is 1 to 6), $-O-(R^8-O)_t-R^{19}$ (where t is 1 to 6), $-O-R^8-C(O)R^5$, $-O-R^8-C(O)R^{19}$, $-O-R^8-C(O)OR^5$, $-N(R^5)-R^8-N(R^{19})R^{11}$, $-S(O)_p-R^8-N(R^5)R^6$ (where p is 0 to 2), $-S(O)_p-R^8-C(O)OR^5$ (where p is 0 to 2), or $-N(R^5)-CH(R^{12})-C(O)OR^5$;

R^3 is aryl or heterocyclyl both substituted by one or more R^{14} substituents independently selected from the group consisting of hydrogen, alkyl, halo, formyl, acetyl, cyano, $-R^8-CN$, $-N(R^{10})R^{11}$, $-R^8-N(R^{10})R^{11}$, $-R^8-N^{\oplus}(R^9)(R^{16})_2$, $-C(O)OR^5$, $-R^8-C(O)OR^5$, $-OR^5$, $-R^8-OR^5$, $-C(R^7)H-O-R^{15}$, $-S(O)_p-R^{15}$ (where p is 0 to 2), $-R^8-S(O)_p-R^{15}$ (where p is 0 to 2), $-S(O)_p-N(R^5)R^6$ (where p is 0 to 2), $-C(O)N(R^5)R^6$, $-R^8-C(O)N(R^5)R^6$, $-N(R^5)-(R^8-O)_t-R^5$ (where t is 1 to 6), $-R^8-N(R^5)-(R^8-O)_t-R^5$ (where t is 1 to 6), $-R^8-O-(R^8-O)_t-R^5$ (where t is 1 to 6), $-O-R^8-CH(OH)-CH_2-OR^5$, $-C(R^7)H-O-R^8-CH(OH)-CH_2-OR^5$, $-C(R^7)H-N(R^5)-R^8-[CH(OH)]_t-CH_2-OR^5$ (where t is 1 to 6), $-C(R^7)H-N(R^5)-S(O)_2-N(R^{10})R^{11}$, $-C(R^7)H-N(R^{10})-C(NR^{17})-N(R^{10})R^{11}$, $-C(R^7)H-N(R^{10})-C(NR^{17})-R^{10}$, $-C(NR^{17})-N(R^5)R^6$, $-C(R^7)H-C(NR^{17})-N(R^5)R^6$, $-C(R^7)H-O-N(R^5)R^6$, heterocyclyl (wherein the heterocyclyl radical is not attached to the rest of the molecule through a nitrogen atom and is optionally substituted by alkyl, aryl, aralkyl, halo, haloalkyl, oxo, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ or $-C(O)N(R^5)R^6$), and heterocyclylalkyl (wherein the heterocyclyl radical is not attached to the alkyl radical through a nitrogen ring and is optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, oxo, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ and $-C(O)N(R^5)R^6$);

each R^4 is independently hydrogen, alkyl, halo, haloalkyl, cyano, nitro, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^8$, $-C(O)N(R^5)R^6$, or $-R^8-N(R^5)R^6$;

each R^5 and R^8 is independently hydrogen, alkyl, aryl or aralkyl;

each R^7 is independently hydrogen or alkyl;

each R^8 is independently a straight or branched alkylene, alkylidene or alkylidyne chain;

each R^9 is independently alkyl, aryl or aralkyl;

each R^{10} and R^{11} is independently hydrogen, alkyl, haloalkyl, aryl, aralkyl, formyl, cyano, $-R^8-CN$,

$-OR^5$, $-R^8-OR^5$, $-S(O)_p-R^{15}$ (where p is 0 to 2), $-R^8-S(O)_p-R^{15}$ (where p is 0 to 2), $-N(R^5)R^6$, $-R^8-N(R^5)R^6$, $-R^8-C(O)OR^5$, $-C(O)-R^{15}$, $-C(O)NH_2$, $-R^8-C(O)NH_2$, $-C(S)NH_2$, $-C(O)-S-R^5$, $-C(O)-N(R^5)R^{15}$, $-R^8-C(O)-N(R^5)R^{15}$, $-C(S)-N(R^5)R^{15}$, $-R^8-N(R^5)-C(O)H$, $-R^8-N(R^5)-C(O)R^{15}$, $-C(O)O-R^8-N(R^5)R^6$, $-C(N(R^5)R^5)=C(R^{15})R^{10}$, $-R^8-N(R^5)-P(O)(OR^5)_2$, cycloalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, halo and $-OR^5$), heterocyclyl (optionally substituted by alkyl, aryl, aralkyl, halo, haloalkyl, oxo, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-S(O)_p-R^9$ (where p is 0 to 2), $-R^8-S(O)_p-R^9$ (where p is 0 to 2), $-N(R^5)R^6$ or $-C(O)N(R^5)R^6$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, oxo, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-S(O)_p-R^9$ (where p is 0 to 2), $-R^8-S(O)_p-R^9$ (where p is 0 to 2), $-N(R^5)R^6$ and $-C(O)N(R^5)R^6$);

or R^{10} and R^{11} together with the nitrogen to which they are attached form a *N*-heterocyclic ring containing zero to three additional hetero atoms, where the *N*-heterocylic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, halo, haloalkyl, aryl, aralkyl, oxo, nitro, cyano, $-R^8-CN$, $=N(R^{17})$, $-OR^5$, $-C(O)OR^5$, $-R^8-C(O)OR^5$, $-N(R^5)R^6$, $-R^8-N(R^5)R^6$, $-C(O)N(R^5)R^6$, $-R^8-C(O)N(R^5)R^6$, $-N(R^5)-N(R^5)R^6$, $-C(O)R^5$, $-C(O)-(R^8-O)_t-R^5$ (where t is 1 to 6), $-S(O)_p-R^9$ (where p is 0 to 2), $-R^8-S(O)_p-R^9$ (where p is 0 to 2), $-(R^8-O)_t-R^5$ (where t is 1 to 6), and heterocyclyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$, and $-C(O)N(R^5)R^6$);

R^{12} is a side chain of an α-amino acid;

each R^{15} is independently alkyl, cycloalkyl, haloalkyl, aryl, aralkyl, $-R^8-O-C(O)-R^5$, $-R^8-OR^5$, $-N(R^5)R^6$, $-R^8-N(R^5)R^6$, $-R^8-C(O)OR^5$, heterocyclyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$, and $-C(O)N(R^5)R^6$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$, and $-C(O)N(R^5)R^5$);

or R^5 and R^{15} together with the nitrogen to which they are attached form a *N*-heterocyclic ring containing zero to three additional hetero atoms, where the *N*-heterocyclic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, amino, monoalkylamino, dialkylamino, OR^5, $-C(O)OR^5$, aminocarbonyl, monoalkylaminocarbonyl, and dialkylaminocarbonyl;

each R^{16} is independently alkyl, aryl, aralkyl, $-R^8-OR^5$, $-R^8-N(R^5)R^6$, cycloalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, halo and $-OR^5$), heterocyclyl (optionally substituted by alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$,

$-C(O)OR^5$, $-N(R^5)R^6$ or $-C(O)N(R^5)R^6$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ and $-C(O)N(R^5)R^6$); or

both R^{16}s together with the nitrogen to which they are attached (and wherein the R^9 substituent is not present) form an aromatic *N*-heterocyclic ring containing zero to three additional hetero atoms, where the *N*-heterocylic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-R^8-C(O)OR^5$, $-N(R^5)R^6$, $-R^8-N(R^5)R^6$, $-C(O)R^5$, $-C(O)-(R^8-O)_t-R^5$ (where t is 1 to 6), and $-(R^8-O)_t-R^5$ (where t is 1 to 6);

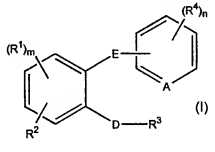
each R^{17} is independently hydrogen, alkyl, aryl, aralkyl, cyano, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-R^8-C(O)OR^5$, $-C(O)-N(R^5)R^6$, or $-R^8-C(O)-N(R^5)R^6$;

R^{18} is hydrogen, alkyl, aryl, aralkyl, cyano, $-C(O)OR^5$, or $-NO_2$; and

each R^{19} is cycloalkyl, haloalkyl, $-R^8-OR^5$, $-R^8-N(R^5)R^6$, $-R^8-C(O)OR^5$, $-R^8-C(O)N(R^5)R^6$, heterocyclyl (optionally substituted by alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^8$ or $-C(O)N(R^5)R^6$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ and $-C(O)N(R^5)R^6$);

as a single stereoisomer or a mixture thereof; or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

67. The pharmaceutical composition of Claim 66 wherein the composition comprises a therapeutically effective amount of a compound of formula (I):



(I)

A is =CH- or =N-;

m is 1 to 3;

n is 1 to 4;

D is $-N(R^5)-C(Z)-$ or $-N(R^5)-S(O)_p-$ (where p is 0 to 2; Z is oxygen, sulfur or H_2; and the nitrogen atom is directly bonded to the phenyl ring having the R^1 and R^2 substituents);

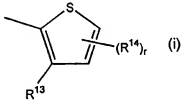
E is -C(Z)-N(R^5)- or -S(O)$_p$-N(R^5)- (where p is 0 to 2; Z is oxygen, sulfur or H_2; and the nitrogen atom can be bonded to the phenyl ring having the R^1 and the R^2 substituents or to the aromatic ring having the R^4 substituent);

each R^1 is independently hydrogen, alkyl, aryl, aralkyl, halo, haloalkyl, cyano, -OR^5, -S(O)$_p$-R^9 (where p is 0 to 2), -C(O)OR^5, -C(O)N(R^5)R^6, -N(R^5)R^6, -O-C(O)R^5, or -N(R^5)-CH(R^{12})-C(O)OR^5;

or two adjacent R^1's together with the carbons to which they are attached form a heterocyclic ring fused to the phenyl ring wherein the heterocyclic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl and aralkyl;

R^2 is hydrogen, alkyl, aryl, aralkyl, halo, haloalkyl, cyano, -OR^5, -S(O)$_p$-R^8 (where p is 0 to 2), -C(O)OR^5, -C(O)N(R^5)R^6, -N(R^{10})R^{11}, -C(R^7)H-N(R^{10})R^{11}, -C(R^7)H-R^8-N(R^{10})R^{11}, -C(R^7)H-OR^5, -C(R^7)H-R^8-OR^5, -C(R^7)H-S(O)$_p$-R^9 (where p is 0 to 2), -C(R^7)H-R^8-S(O)$_p$-R^9 (where p is 0 to 2), -O-R^8-S(O)$_p$-R^9 (where p is 0 to 2), -C(R^7)H-N(R^5)R^6, -C(R^7)H-R^8-N(R^5)R^6, -O-R^8-CH(OH)-CH_2-N(R^{10})R^{11}, -O-R^8-N(R^{10})R^{11}, -O-R^8-O-C(O)R^5, -O-R^8-CH(OH)-CH_2-OR^5, -O-(R^8-O)$_t$-R^5 (where t is 1 to 6), -O-(R^8-O)$_t$-R^{19} (where t is 1 to 6), -O-R^8-C(O)R^5, -O-R^8-C(O)R^{19}, -O-R^8-C(O)OR^5, -N(R^5)-R^8-N(R^{10})R^{11}, -S(O)$_p$-R^8-N(R^5)R^6 (where p is 0 to 2), -S(O)$_p$-R^8-C(O)OR^5 (where p is 0 to 2), or -N(R^5)-CH(R^{12})-C(O)OR^5;

R^3 is a radical of formula (i):



(i)

where:

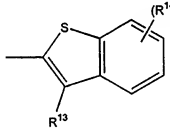
r is 1 or 2;

R^{13} is hydrogen, alkyl, halo, haloalkyl, -N(R^5)R^6, -C(R^7)H-N(R^5)R^8, -OR^5, -R^8-OR^5, -S(O)$_p$-R^8-N(R^5)R^6 (where p is 0 to 2) or heterocyclylalkyl (where the heterocyclic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, halo, aralkyl, nitro and cyano); and

each R^{14} is independently hydrogen, alkyl, halo, formyl, acetyl, cyano, -R^8-CN, -N(R^{10})R^{11}, -C(R^7)H-N(R^{10})R^{11}, -C(R^7)H-R^8-N(R^{10})R^{11}, -C(R^7)H-N$^{\oplus}$(R^5)(R^{16})$_2$, -C(R^7)H-R^8-N$^{\oplus}$(R^5)(R^{16})$_2$, -C(O)OR^5, -C(R^7)H-C(O)OR^5, -C(R^7)H-R^8-C(O)OR^5,

$-OR^5$, $-C(R^7)H-OR^5$, $-C(R^7)H-R^8-OR^5$, $-C(R^7)H-O-R^{15}$, $-S(O)_p-R^{15}$ (where p is 0 to 2), $-C(R^7)H-S(O)_p-R^{15}$ (where p is 0 to 2), $-C(R^7)H-R^8-S(O)_p-R^{15}$ (where p is 0 to 2), $-S(O)_p-N(R^5)R^6$ (where p is 0 to 2), $-C(O)N(R^5)R^6$, $-C(R^7)H-C(O)N(R^5)R^6$, $-C(R^7)H-R^8-C(O)N(R^5)R^6$, $-C(R^7)H-N(R^5)-(R^8-O)_t-R^5$ (where t is 1 to 6), $-C(R^7)H-R^8-N(R^5)-(R^8-O)_t-R^5$ (where t is 1 to 6), $-C(R^7)H-O-(R^8-O)_t-R^5$ (where t is 1 to 6), $-C(R^7)H-R^8-O-(R^8-O)_t-R^5$ (where t is 1 to 6), $-O-R^8-CH(OH)-CH_2-OR^5$, $-C(R^7)H-O-R^8-CH(OH)-CH_2-OR^5$, $-C(R^7)H-N(R^5)-R^8-[CH(OH)]_t-CH_2-OR^5$ (where t is 1 to 6), $-C(R^7)H-N(R^5)-S(O)_2-N(R^{10})R^{11}$, $-C(R^7)H-N(R^{10})-C(NR^{17})-N(R^{10})R^{11}$, $-C(R^7)H-N(R^{10})-C(NR^{17})-R^{10}$, $-C(NR^{17})-N(R^5)R^6$, $-C(R^7)H-C(NR^{17})-N(R^5)R^6$, $-C(R^7)H-O-N(R^5)R^6$, heterocyclyl (wherein the heterocyclyl radical is not attached to the radical of formula (i) through a nitrogen atom and is optionally substituted by alkyl, aryl, aralkyl, halo, haloalkyl, oxo, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ or $-C(O)N(R^5)R^6$), or heterocyclylalkyl (wherein the heterocyclyl radical is not attached to the alkyl radical through a nitrogen atom and is optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, oxo, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ and $-C(O)N(R^5)R^6$);

or R^3 is a radical of the formula (ii):



(ii)

where v is 1 to 4;

R^{13} is as defined above for formula (i); and

R^{14} is as defined above for formula (i);

each R^4 is independently hydrogen, alkyl, halo, haloalkyl, cyano, nitro, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$, $-C(O)N(R^5)R^6$, or $-R^8-N(R^5)R^6$;

R^5 and R^6 are each independently hydrogen, alkyl, aryl or aralkyl;

each R^7 is independently hydrogen or alkyl;

each R^8 is independently a straight or branched alkylene, alkylidene or alkylidyne chain;

each R^9 is independently alkyl, aryl or aralkyl;

R^{10} and R^{11} are each independently hydrogen, alkyl, haloalkyl, aryl, aralkyl, formyl, cyano, $-R^8-CN$,

$-OR^5$, $-R^8-OR^5$, $-S(O)_p-R^{15}$ (where p is 0 to 2), $-R^8-S(O)_p-R^{15}$ (where p is 0 to 2), $-N(R^5)R^6$, $-R^8-N(R^5)R^6$, $-R^8-C(O)OR^5$, $-C(O)-R^{15}$, $-C(O)NH_2$, $-R^8-C(O)NH_2$, $-C(S)NH_2$, $-C(O)-S-R^5$, $-C(O)-N(R^5)R^{15}$, $-R^8-C(O)-N(R^5)R^{15}$, $-C(S)-N(R^5)R^{15}$, $-R^8-N(R^5)-C(O)H$, $-R^8-N(R^5)-C(O)R^{15}$, $-C(O)O-R^8-N(R^5)R^6$, $-C(N(R^5)R^6)=C(R^{18})R^{10}$, $-R^8-N(R^5)-P(O)(OR^5)_2$, cycloalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, halo and $-OR^5$), heterocyclyl (optionally substituted by alkyl, aryl, aralkyl, halo, haloalkyl, oxo, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-S(O)_p-R^9$ (where p is 0 to 2), $-R^8-S(O)_p-R^9$ (where p is 0 to 2), $-N(R^5)R^6$ or $-C(O)N(R^5)R^6$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, oxo, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-S(O)_p-R^9$ (where p is 0 to 2), $-R^8-S(O)_p-R^9$ (where p is 0 to 2), $-N(R^5)R^6$ and $-C(O)N(R^5)R^6$);

or R^{10} and R^{11} together with the nitrogen to which they are attached form a *N*-heterocyclic ring containing zero to three additional hetero atoms, where the *N*-heterocylic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, halo, haloalkyl, aryl, aralkyl, oxo, nitro, cyano, $-R^8-CN$, $=N(R^{17})$, $-OR^5$, $-C(O)OR^5$, $-R^8-C(O)OR^5$, $-N(R^5)R^6$, $-R^8-N(R^5)R^6$, $-C(O)N(R^5)R^6$, $-R^8-C(O)N(R^5)R^6$, $-N(R^5)-N(R^5)R^6$, $-C(O)R^5$, $-C(O)-(R^8-O)_t-R^5$ (where t is 1 to 6), $-S(O)_p-R^9$ (where p is 0 to 2), $-R^8-S(O)_p-R^9$ (where p is 0 to 2), $-(R^8-O)_t-R^5$ (where t is 1 to 6), and heterocyclyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$, and $-C(O)N(R^5)R^6$);

R^{12} is a side chain of an α-amino acid;

each R^{15} is independently alkyl, cycloalkyl, haloalkyl, aryl, aralkyl, $-R^8-O-C(O)-R^5$, $-R^8-OR^5$, $-N(R^5)R^6$, $-R^8-N(R^5)R^6$, $-R^8-C(O)OR^5$, heterocyclyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$, and $-C(O)N(R^5)R^6$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$, and $-C(O)N(R^5)R^6$);

or R^5 and R^{15} together with the nitrogen to which they are attached form a *N*-heterocyclic ring containing zero to three additional hetero atoms, where the *N*-heterocyclic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, amino, monoalkylamino, dialkylamino, $-OR^5$, $-C(O)OR^5$, aminocarbonyl, monoalkylaminocarbonyl, and dialkylaminocarbonyl;

each R^{16} is independently alkyl, aryl, aralkyl, $-R^8-OR^5$, $-R^8-N(R^5)R^6$, cycloalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, halo and $-OR^5$), heterocyclyl (optionally substituted by alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$,

-C(O)OR^5, -N(R^5)R^6 or -C(O)N(R^5)R^6), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, -OR^5, -C(O)OR^5, -N(R^5)R^6 and -C(O)N(R^5)R^6); or

both R^{16}'s together with the nitrogen to which they are attached (and wherein the R^9 substituent is not present) form an aromatic *N*-heterocyclic ring containing zero to three additional hetero atoms, where the *N*-heterocylic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, -OR^5, -C(O)OR^5, -R^8-C(O)OR^5, -N(R^5)R^6, -R^8-N(R^5)R^6, -C(O)R^5, -C(O)-(R^8-O)$_t$-R^5 (where t is 1 to 6), and -(R^8-O)$_t$-R^5 (where t is 1 to 6);

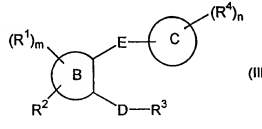
each R^{17} is independently hydrogen, alkyl, aryl, aralkyl, cyano, -OR^5, -R^8-OR^5, -C(O)OR^5, -R^8-C(O)OR^5, or -R^8-C(O)-N(R^5)R^6;

R^{18} is hydrogen, alkyl, aryl, aralkyl, cyano, -C(O)OR^5, or -NO$_2$; and

each R^{19} is cycloalkyl, haloalkyl, -R^8-OR^5, -R^8-N(R^5)R^6, -R^8-C(O)OR^5, -R^8-C(O)N(R^5)R^6, heterocyclyl (optionally substituted by alkyl, aryl, aralkyl, halo, haloalkyl, -OR^5, -C(O)OR^5, -N(R^5)R^6 or -C(O)N(R^5)R^6), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, -OR^5, -C(O)OR^5, -N(R^5)R^6 and -C(O)N(R^5)R^6);

as a single stereoisomer or a mixture thereof; or a pharmaceutically acceptable salt thereof; and a pharmaceutically acceptable excipient.

68. A method of treating a human having a disease-state characterized by thrombotic activity, which method comprises administering to a human in need thereof a therapeutically effective amount of a compound of formula (III):

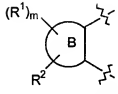


(III)

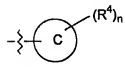
wherein

m is 1 to 3;

n is 1 to 5;



is an aryl or a heterocyclic ring substituted by R^2 and one or more R^1 groups;



is an aryl or a heterocyclic ring substituted by one or more R^4 groups;

D and E are independently a linker selected from the group consisting of -N(R^5)-C(X)-; -R^8-N(R^5)-C(X)-; -N(R^5)-C(X)-R^8-; -R^8-N(R^5)-C(X)-R^8- ; -N(R^5)-S(O)$_p$-; -R^8-N(R^5)-S(O)$_p$-; -N(R^5)-S(O)$_p$-R^8- ; and -R^8-N(R^5)-S(O)$_p$-R^8- (where p is 0 to 2; X is oxygen, sulfur or H_2) where D and E can be attached to the B ring having the R^1 and R^2 substituents by either terminus of the linker;

each R^1 is independently hydrogen, alkyl, aryl, aralkyl, halo, haloalkyl, cyano, -OR^5, -S(O)$_p$-R^9 (where p is 0 to 2), -C(O)OR^5, -C(O)N(R^5)R^8, -N(R^5)R^6, -O-C(O)R^5, -N(R^5)-CH(R^{12})-C(O)OR^5, heterocyclyl (optionally substituted by alkyl, aryl, aralkyl, halo, haloalkyl, oxo, -OR^5, -C(O)OR^5, -N(R^5)R^8 or -C(O)N(R^5)R^6) or heterocyclylalkyl (optionally substituted by alkyl, aryl, aralkyl, halo, haloalkyl, oxo, -OR^5, -C(O)OR^5, -N(R^5)R^8 or -C(O)N(R^5)R^6);

R^2 is hydrogen, alkyl, aryl, aralkyl, halo, haloalkyl, cyano, -OR^5, -S(O)$_p$-R^9 (where p is 0 to 2), -C(O)OR^5, -C(O)N(R^5)R^8, -N(R^{10})R^{11}, -C(R^7)H-N(R^{10})R^{11}, -C(R^7)H-R^8-N(R^{10})R^{11}, -C(R^7)H-OR^5, -C(R^7)H-R^8-OR^5, -C(R^7)H-S(O)$_p$-R^9 (where p is 0 to 2), -C(R^7)H-R^8-S(O)$_p$-R^9 (where p is 0 to 2), -O-R^8-S(O)$_p$-R^9 (where p is 0 to 2), -C(R^7)H-N(R^5)R^6, -C(R^7)H-R^8-N(R^5)R^8, -O-R^8-CH(OH)-CH_2-N(R^{10})R^{11}, -O-R^8-N(R^{10})R^{11}, -O-R^8-O-C(O)R^5, -O-R^8-CH(OH)-CH_2-OR^5, -O-(R^8-O)$_t$-R^5 (where t is 1 to 6), -O-(R^8-O)$_t$-R^{19} (where t is 1 to 6), -O-R^8-C(O)R^5, -O-R^8-C(O)R^{19}, -O-R^8-C(O)OR^5, -N(R^5)-R^8-N(R^{10})R^{11}, -S(O)$_p$-R^8-N(R^5)R^6 (where p is 0 to 2), -S(O)$_p$-R^8-C(O)OR^5 (where p is 0 to 2), or -N(R^5)-CH(R^{12})-C(O)OR^5;

R^3 is aryl or heterocyclyl both substituted by one or more R^{14} substituents independently selected from the group consisting of hydrogen, alkyl, halo, formyl, acetyl, cyano, -R^8-CN, -N(R^{10})R^{11}, -R^8-N(R^{10})R^{11}, -R^8-$N^{\oplus}$(R^9)(R^{16})$_2$, -C(O)OR^5, -R^8-C(O)OR^5, -OR^5, -R^8-OR^5, -C(R^7)H-O-R^{15}, -S(O)$_p$-R^{15} (where p is 0 to 2), -R^8-S(O)$_p$-R^{15} (where p is 0 to 2), -S(O)$_p$-N(R^5)R^6 (where p is 0 to 2), -C(O)N(R^5)R^6, -R^8-C(O)N(R^5)R^6, -N(R^5)-(R^8-O)$_t$-R^5 (where t is 1 to 6), -R^8-N(R^5)-(R^8-O)$_t$-R^5 (where t is 1 to 6), -R^8-O-(R^8-O)$_t$-R^5 (where t is 1 to 6), -O-R^8-CH(OH)-CH_2-OR^5, -C(R^7)H-O-R^8-CH(OH)-CH_2-OR^5,

$-C(R^7)H-N(R^5)-R^8-[CH(OH)]_t-CH_2-OR^5$ (where t is 1 to 6), $-C(R^7)H-N(R^5)-S(O)_2-N(R^{10})R^{11}$, $-C(R^7)H-N(R^{10})-C(NR^{17})-N(R^{10})R^{11}$, $-C(R^7)H-N(R^{10})-C(NR^{17})-R^{10}$, $-C(NR^{17})-N(R^5)R^8$, $-C(R^7)H-C(NR^{17})-N(R^5)R^8$, $-C(R^7)H-O-N(R^5)R^8$, heterocyclyl (wherein the heterocyclyl radical is not attached to the rest of the molecule through a nitrogen atom and is optionally substituted by alkyl, aryl, aralkyl, halo, haloalkyl, oxo, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ or $-C(O)N(R^5)R^6$), and heterocyclylalkyl (wherein the heterocyclyl radical is not attached to the alkyl radical through a nitrogen ring and is optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, oxo, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ and $-C(O)N(R^5)R^6$);

each R^4 is independently hydrogen, alkyl, halo, haloalkyl, cyano, nitro, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$, $-C(O)N(R^5)R^6$, or $-R^8-N(R^5)R^8$;

each R^5 and R^8 is independently hydrogen, alkyl, aryl or aralkyl;

each R^7 is independently hydrogen or alkyl;

each R^8 is independently a straight or branched alkylene, alkylidene or alkylidyne chain;

each R^9 is independently alkyl, aryl or aralkyl;

each R^{10} and R^{11} is independently hydrogen, alkyl, haloalkyl, aryl, aralkyl, formyl, cyano, $-R^8-CN$, $-OR^5$, $-R^8-OR^5$, $-S(O)_p-R^{15}$ (where p is 0 to 2), $-R^8-S(O)_p-R^{15}$ (where p is 0 to 2), $-N(R^5)R^6$, $-R^8-N(R^5)R^8$, $-R^8-C(O)OR^5$, $-C(O)-R^{15}$, $-C(O)NH_2$, $-R^8-C(O)NH_2$, $-C(S)NH_2$, $-C(O)-S-R^5$, $-C(O)-N(R^5)R^{15}$, $-R^8-C(O)-N(R^5)R^{15}$, $-C(S)-N(R^5)R^{15}$, $-R^8-N(R^5)-C(O)H$, $-R^8-N(R^5)-C(O)R^{15}$, $-C(O)O-R^8-N(R^5)R^8$, $-C(N(R^5)R^6)=C(R^{18})R^{10}$, $-R^8-N(R^5)-P(O)(OR^5)_2$, cycloalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, halo and $-OR^5$), heterocyclyl (optionally substituted by alkyl, aryl, aralkyl, halo, haloalkyl, oxo, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-S(O)_p-R^9$ (where p is 0 to 2), $-R^8-S(O)_p-R^9$ (where p is 0 to 2), $-N(R^5)R^6$ or $-C(O)N(R^5)R^6$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, oxo, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-S(O)_p-R^9$ (where p is 0 to 2), $-R^8-S(O)_p-R^9$ (where p is 0 to 2), $-N(R^5)R^6$ and $-C(O)N(R^5)R^6$);

or R^{10} and R^{11} together with the nitrogen to which they are attached form a *N*-heterocyclic ring containing zero to three additional hetero atoms, where the *N*-heterocylic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, halo, haloalkyl, aryl, aralkyl, oxo, nitro, cyano, $-R^8-CN$, $=N(R^{17})$, $-OR^5$, $-C(O)OR^5$, $-R^8-C(O)OR^5$, $-N(R^5)R^6$, $-R^8-N(R^5)R^6$, $-C(O)N(R^5)R^6$, $-R^8-C(O)N(R^5)R^6$, $-N(R^5)-N(R^5)R^6$, $-C(O)R^5$, $-C(O)-(R^8-O)_t-R^5$ (where t is 1 to 6), $-S(O)_p-R^9$ (where p is 0 to 2), $-R^8-S(O)_p-R^9$ (where p is 0 to 2), $-(R^8-O)_t-R^5$ (where t is 1 to 6), and heterocyclyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl,

$-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$, and $-C(O)N(R^5)R^6$);

R^{12} is a side chain of an α-amino acid;

each R^{15} is independently alkyl, cycloalkyl, haloalkyl, aryl, aralkyl, $-R^8-O-C(O)-R^5$, $-R^8-OR^5$, $-N(R^5)R^6$, $-R^8-N(R^5)R^6$, $-R^8-C(O)OR^5$, heterocyclyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$, and $-C(O)N(R^5)R^6$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$, and $-C(O)N(R^5)R^6$);

or R^5 and R^{15} together with the nitrogen to which they are attached form a *N*-heterocyclic ring containing zero to three additional hetero atoms, where the *N*-heterocyclic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, amino, monoalkylamino, dialkylamino, OR^5, $-C(O)OR^5$, aminocarbonyl, monoalkylaminocarbonyl, and dialkylaminocarbonyl;

each R^{16} is independently alkyl, aryl, aralkyl, $-R^8-OR^5$, $-R^8-N(R^5)R^6$, cycloalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, halo and $-OR^5$), heterocyclyl (optionally substituted by alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ or $-C(O)N(R^5)R^6$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ and $-C(O)N(R^5)R^6$); or

both R^{16}s together with the nitrogen to which they are attached (and wherein the R^9 substituent is not present) form an aromatic *N*-heterocyclic ring containing zero to three additional hetero atoms, where the *N*-heterocylic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-R^8-C(O)OR^5$, $-N(R^5)R^6$, $-R^8-N(R^5)R^6$, $-C(O)R^5$, $-C(O)-(R^8-O)_t-R^5$ (where t is 1 to 6), and $-(R^8-O)_t-R^5$ (where t is 1 to 6);

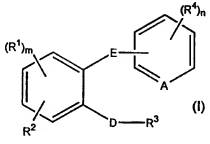
each R^{17} is independently hydrogen, alkyl, aryl, aralkyl, cyano, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-R^8-C(O)OR^5$, $-C(O)-N(R^5)R^6$, or $-R^8-C(O)-N(R^5)R^6$;

R^{18} is hydrogen, alkyl, aryl, aralkyl, cyano, $-C(O)OR^5$, or $-NO_2$; and

each R^{19} is cycloalkyl, haloalkyl, $-R^8-OR^5$, $-R^8-N(R^5)R^6$, $-R^8-C(O)OR^5$, $-R^8-C(O)N(R^5)R^6$, heterocyclyl (optionally substituted by alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ or $-C(O)N(R^5)R^6$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ and $-C(O)N(R^5)R^6$);

as a single stereoisomer or a mixture thereof; or a pharmaceutically acceptable salt thereof.

69. The method of Claim 68 wherein the method comprises administering to a human in need thereof a therapeutically effective amount of a compound of formula (I):



(I)

A is =CH- or =N-;

m is 1 to 3;

n is 1 to 4;

D is $-N(R^5)-C(Z)-$ or $-N(R^5)-S(O)_p-$ (where p is 0 to 2; Z is oxygen, sulfur or H_2; and the nitrogen atom is directly bonded to the phenyl ring having the R^1 and R^2 substituents);

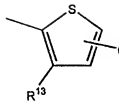
E is $-C(Z)-N(R^5)-$ or $-S(O)_p-N(R^5)-$ (where p is 0 to 2; Z is oxygen, sulfur or H_2; and the nitrogen atom can be bonded to the phenyl ring having the R^1 and the R^2 substituents or to the aromatic ring having the R^4 substituent);

each R^1 is independently hydrogen, alkyl, aryl, aralkyl, halo, haloalkyl, cyano, $-OR^5$, $-S(O)_p-R^9$ (where p is 0 to 2), $-C(O)OR^5$, $-C(O)N(R^5)R^6$, $-N(R^5)R^6$, $-O-C(O)R^5$, or $-N(R^5)-CH(R^{12})-C(O)OR^5$;

or two adjacent R^1's together with the carbons to which they are attached form a heterocyclic ring fused to the phenyl ring wherein the heterocyclic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl and aralkyl;

R^2 is hydrogen, alkyl, aryl, aralkyl, halo, haloalkyl, cyano, $-OR^5$, $-S(O)_p-R^9$ (where p is 0 to 2), $-C(O)OR^5$, $-C(O)N(R^5)R^6$, $-N(R^{10})R^{11}$, $-C(R^7)H-N(R^{10})R^{11}$, $-C(R^7)H-R^8-N(R^{10})R^{11}$, $-C(R^7)H-OR^5$, $-C(R^7)H-R^8-OR^5$, $-C(R^7)H-S(O)_p-R^9$ (where p is 0 to 2), $-C(R^7)H-R^8-S(O)_p-R^9$ (where p is 0 to 2), $-O-R^8-S(O)_p-R^9$ (where p is 0 to 2), $-C(R^7)H-N(R^5)R^6$, $-C(R^7)H-R^8-N(R^5)R^6$, $-O-R^8-CH(OH)-CH_2-N(R^{10})R^{11}$, $-O-R^8-N(R^{10})R^{11}$, $-O-R^8-O-C(O)R^5$, $-O-R^8-CH(OH)-CH_2-OR^5$, $-O-(R^8-O)_t-R^5$ (where t is 1 to 6), $-O-(R^8-O)_t-R^{19}$ (where t is 1 to 6), $-O-R^8-C(O)R^5$, $-O-R^8-C(O)R^{19}$, $-O-R^8-C(O)OR^5$, $-N(R^5)-R^8-N(R^{10})R^{11}$, $-S(O)_p-R^8-N(R^5)R^6$ (where p is 0 to 2), $-S(O)_p-R^8-C(O)OR^5$ (where p is 0 to 2), or $-N(R^5)-CH(R^{12})-C(O)OR^5$;

R^3 is a radical of formula (i):



(i)

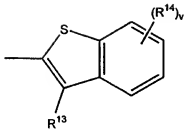
where:

r is 1 or 2;

R^{13} is hydrogen, alkyl, halo, haloalkyl, $-N(R^5)R^5$, $-C(R^7)H-N(R^5)R^6$, $-OR^5$, $-R^8-OR^5$, $-S(O)_p-R^8-N(R^5)R^6$ (where p is 0 to 2) or heterocyclylalkyl (where the heterocyclic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, halo, aralkyl, nitro and cyano); and

each R^{14} is independently hydrogen, alkyl, halo, formyl, acetyl, cyano, $-R^8-CN$, $-N(R^{10})R^{11}$, $-C(R^7)H-N(R^{10})R^{11}$, $-C(R^7)H-R^8-N(R^{10})R^{11}$, $-C(R^7)H-N^{\oplus}(R^9)(R^{16})_2$, $-C(R^7)H-R^8-N^{\oplus}(R^9)(R^{16})_2$, $-C(O)OR^5$, $-C(R^7)H-C(O)OR^5$, $-C(R^7)H-R^8-C(O)OR^5$, $-OR^5$, $-C(R^7)H-OR^5$, $-C(R^7)H-R^8-OR^5$, $-C(R^7)H-O-R^{15}$, $-S(O)_p-R^{15}$ (where p is 0 to 2), $-C(R^7)H-S(O)_p-R^{15}$ (where p is 0 to 2), $-C(R^7)H-R^8-S(O)_p-R^{15}$ (where p is 0 to 2), $-S(O)_p-N(R^5)R^6$ (where p is 0 to 2), $-C(O)N(R^5)R^6$, $-C(R^7)H-C(O)N(R^5)R^6$, $-C(R^7)H-R^8-C(O)N(R^5)R^6$, $-C(R^7)H-N(R^5)-(R^8-O)_t-R^5$ (where t is 1 to 6), $-C(R^7)H-R^8-N(R^5)-(R^8-O)_t-R^5$ (where t is 1 to 6), $-C(R^7)H-O-(R^8-O)_t-R^5$ (where t is 1 to 6), $-C(R^7)H-R^8-O-(R^8-O)_t-R^5$ (where t is 1 to 6), $-O-R^8-CH(OH)-CH_2-OR^5$, $-C(R^7)H-O-R^8-CH(OH)-CH_2-OR^5$, $-C(R^7)H-N(R^5)-R^8-[CH(OH)]_t-CH_2-OR^5$ (where t is 1 to 6), $-C(R^7)H-N(R^5)-S(O)_2-N(R^{10})R^{11}$, $-C(R^7)H-N-(R^{10})-C(NR^{17})-N(R^{10})R^{11}$, $-C(R^7)H-N(R^{10})-C(NR^{17})-R^{10}$, $-C(NR^{17})-N(R^5)R^6$, $-C(R^7)H-C(NR^{17})-N(R^5)R^6$, $-C(R^7)H-O-N(R^5)R^6$, heterocyclyl (wherein the heterocyclyl radical is not attached to the radical of formula (i) through a nitrogen atom and is optionally substituted by alkyl, aryl, aralkyl, halo, haloalkyl, oxo, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ or $-C(O)N(R^5)R^6$), or heterocyclylalkyl (wherein the heterocyclyl radical is not attached to the alkyl radical through a nitrogen atom and is optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, oxo, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ and $-C(O)N(R^5)R^6$);

or R^3 is a radical of the formula (ii):



(ii)

where v is 1 to 4;

R^{13} is as defined above for formula (i); and

R^{14} is as defined above for formula (i);

each R^4 is independently hydrogen, alkyl, halo, haloalkyl, cyano, nitro, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$, $-C(O)N(R^5)R^6$, or $-R^8-N(R^5)R^5$;

R^5 and R^6 are each independently hydrogen, alkyl, aryl or aralkyl;

each R^7 is independently hydrogen or alkyl;

each R^8 is independently a straight or branched alkylene, alkylidene or alkylidyne chain;

each R^9 is independently alkyl, aryl or aralkyl;

R^{10} and R^{11} are each independently hydrogen, alkyl, haloalkyl, aryl, aralkyl, formyl, cyano, $-R^8-CN$, $-OR^5$, $-R^8-OR^5$, $-S(O)_p-R^{15}$ (where p is 0 to 2), $-R^8-S(O)_p-R^{15}$ (where p is 0 to 2), $-N(R^5)R^6$, $-R^8-N(R^5)R^6$, $-R^8-C(O)OR^5$, $-C(O)-R^{15}$, $-C(O)NH_2$, $-R^8-C(O)NH_2$, $-C(S)NH_2$, $-C(O)-S-R^5$, $-C(O)-N(R^5)R^{15}$, $-R^8-C(O)-N(R^5)R^{15}$, $-C(S)-N(R^5)R^{15}$, $-R^8-N(R^5)-C(O)H$, $-R^8-N(R^5)-C(O)R^{15}$, $-C(O)O-R^8-N(R^5)R^6$, $-C(N(R^5)R^6)=C(R^{16})R^{10}$, $-R^8-N(R^5)-P(O)(OR^5)_2$, cycloalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, halo and $-OR^5$), heterocyclyl (optionally substituted by alkyl, aryl, aralkyl, halo, haloalkyl, oxo, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-S(O)_p-R^9$ (where p is 0 to 2), $-R^8-S(O)_p-R^9$ (where p is 0 to 2), $-N(R^5)R^6$ or $-C(O)N(R^5)R^6$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, oxo, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-S(O)_p-R^9$ (where p is 0 to 2), $-R^8-S(O)_p-R^9$ (where p is 0 to 2), $-N(R^5)R^6$ and $-C(O)N(R^5)R^6$);

or R^{10} and R^{11} together with the nitrogen to which they are attached form a *N*-heterocyclic ring containing zero to three additional hetero atoms, where the *N*-heterocylic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, halo, haloalkyl, aryl, aralkyl, oxo, nitro, cyano, $-R^8-CN$, $=N(R^{17})$, $-OR^5$, $-C(O)OR^5$, $-R^8-C(O)OR^5$, $-N(R^5)R^6$, $-R^8-N(R^5)R^6$, $-C(O)N(R^5)R^6$, $-R^8-C(O)N(R^5)R^6$, $-N(R^5)-N(R^5)R^6$, $-C(O)R^5$, $-C(O)-(R^8-O)_t-R^5$ (where t is 1 to 6), $-S(O)_p-R^9$ (where p is 0 to 2), $-R^8-S(O)_p-R^9$ (where p is 0 to 2), $-(R^8-O)_t-R^5$ (where t is 1 to 6), and heterocyclyl (optionally substituted by one or

more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^8$, and $-C(O)N(R^5)R^6$);

R^{12} is a side chain of an α-amino acid;

each R^{15} is independently alkyl, cycloalkyl, haloalkyl, aryl, aralkyl, $-R^8-O-C(O)-R^5$, $-R^8-OR^5$, $-N(R^5)R^8$, $-R^8-N(R^5)R^6$, $-R^8-C(O)OR^5$, heterocyclyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$, and $-C(O)N(R^5)R^6$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$, and $-C(O)N(R^5)R^8$);

or R^5 and R^{15} together with the nitrogen to which they are attached form a *N*-heterocyclic ring containing zero to three additional hetero atoms, where the *N*-heterocyclic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, amino, monoalkylamino, dialkylamino, $-OR^5$, $-C(O)OR^5$, aminocarbonyl, monoalkylaminocarbonyl, and dialkylaminocarbonyl;

each R^{18} is independently alkyl, aryl, aralkyl, $-R^8-OR^5$, $-R^8-N(R^5)R^6$, cycloalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, halo and $-OR^5$), heterocyclyl (optionally substituted by alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ or $-C(O)N(R^5)R^6$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ and $-C(O)N(R^5)R^6$); or

both R^{18}'s together with the nitrogen to which they are attached (and wherein the R^9 substituent is not present) form an aromatic *N*-heterocyclic ring containing zero to three additional hetero atoms, where the *N*-heterocylic ring is optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, $-OR^5$, $-C(O)OR^5$, $-R^8-C(O)OR^5$, $-N(R^5)R^6$, $-R^8-N(R^5)R^6$, $-C(O)R^5$, $-C(O)-(R^8-O)_t-R^5$ (where t is 1 to 6), and $-(R^8-O)_t-R^5$ (where t is 1 to 6);

each R^{17} is independently hydrogen, alkyl, aryl, aralkyl, cyano, $-OR^5$, $-R^8-OR^5$, $-C(O)OR^5$, $-R^8-C(O)OR^5$, $-C(O)-N(R^5)R^6$, or $-R^8-C(O)-N(R^5)R^6$;

R^{18} is hydrogen, alkyl, aryl, aralkyl, cyano, $-C(O)OR^5$, or $-NO_2$; and

each R^{19} is cycloalkyl, haloalkyl, $-R^8-OR^5$, $-R^8-N(R^5)R^6$, $-R^8-C(O)OR^5$, $-R^8-C(O)N(R^5)R^8$, heterocyclyl (optionally substituted by alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^6$ or $-C(O)N(R^5)R^6$), or heterocyclylalkyl (optionally substituted by one or more substituents selected from the group consisting of alkyl, aryl, aralkyl, halo, haloalkyl, $-OR^5$, $-C(O)OR^5$, $-N(R^5)R^8$ and $-C(O)N(R^5)R^5$);

as a single stereoisomer or a mixture thereof; or a pharmaceutically acceptable salt thereof.

INTERNATIONAL SEARCH REPORT

Int. tional Application No
PCT/EP 98/07650

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 C07D333/38 A61K31/38 A61K31/415 A61K31/495 A61K31/435
C07D409/12 C07D409/14 C07D413/14 C07D417/14 C07D333/70
C07D409/06 C07D473/06 C07D473/34

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 C07D A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of date base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 96 28427 A (BERLEX LAB ;BUCKMAN BRAD O (US); DAVEY DAVID D (US); GUILFORD WILL) 19 September 1996 see abstract; claim 1 see page 1, line 5 - page 2, line 26	1,66,68
A	EP 0 540 051 A (DAIICHI SEIYAKU CO) 5 May 1993 cited in the application see abstract; claim 1 see page 87, line 21 - line 45 see page 88; table 2 see page 58; example 1 see page 68 - page 69; examples 46-48	1,66,68

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
21 May 1999	02/06/1999

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Paisdor, B

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Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

...ernational application No.
PCT/EP 98/ 07650

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 68-69
because they relate to subject matter not required to be searched by this Authority, namely:
Remark: Although claims 68-69
are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [X] Claims Nos.: not applicable
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Claims Nos.: not applicable

In view of the extremely broad Markush claims, the search was executed with due regard to the PCT Search Guidelines (PCT/GL/2), C-111, paragraph 2.1, 2.3 read in conjunction with 3.7 and Rule 33.3 PCT, i.e. particular emphasis was put on the inventive concept, as illustrated by claim 2 and the examples.
The international search was, in so far as possible and reasonable, complete in that it covered the entire subject-matter to which the claims are directed.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Int dional Application No
PCT/EP 98/07650

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9628427 A	19-09-1996	US 5691364 A	25-11-1997
		AU 5299496 A	02-10-1996
		CA 2214685 A	19-09-1996
		EP 0813525 A	29-12-1997
		US 5883100 A	16-03-1999
		US 5877181 A	02-03-1999
		US 5889005 A	30-03-1997
EP 0540051 A	05-05-1993	AT 136293 T	15-04-1996
		AU 666137 B	01-02-1996
		AU 2747092 A	06-05-1993
		CA 2081836 A	01-05-1993
		CN 1072677 A	02-06-1993
		CN 1168885 A	31-12-1997
		CN 1168886 A	31-12-1997
		CZ 284381 B	11-11-1998
		DE 69209615 D	09-05-1996
		DE 69209615 T	09-01-1997
		DK 540051 T	06-05-1996
		ES 2088073 T	01-08-1996
		FI 924932 A	01-05-1993
		GR 3019832 T	31-08-1996
		HK 1002999 A	30-09-1998
		HR 921147 A	31-10-1995
		HU 65890 A	28-07-1994
		IL 103564 A	06-12-1998
		JP 10291931 A	04-11-1998
		JP 5208946 A	20-08-1993
		MX 9206295 A	01-08-1993
		NO 302948 B	11-05-1998
		NZ 244936 A	26-05-1995
		PL 170312 B	29-11-1996
		US 5576343 A	19-11-1996
		US 5620991 A	15-04-1997
		US 5866577 A	02-02-1999
		ZA 9208276 A	06-05-1993
WO 9729067 A	14-08-1997	AU 1454897 A	28-08-1997
		CA 2245925 A	14-08-1997
		CZ 9802550 A	13-01-1999
		EP 0888271 A	07-01-1999
		NO 983671 A	11-09-1998
		PL 328412 A	18-01-1999
WO 9900121 A	07-01-1999	AU 8270898 A	19-01-1999

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
A	WO 97 29067 A (BERLEX LAB) 14 August 1997 cited in the application see abstract; claims see page 39 - page 40; example 1A	1,66,68
E	WO 99 00121 A (BEIGHT DOUGLAS WADE ;GOODSON THEODORE JR (US); HERRON DAVID KENT () 7 January 1999 see abstract; claims see page 62; example 22 see page 64; example 24 see page 54; example 92 see page 78; example 125 see page 98; example 145 see page 118; example 166 see page 161; example 209 see page 162; example 210 see page 193; example 242 see page 226; example 280	1-69

2